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SOCIETY FOR VASCULAR SURGERY

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PER

SURGERY

A Monthly Journal Devoted to the Art and Science of Surgery

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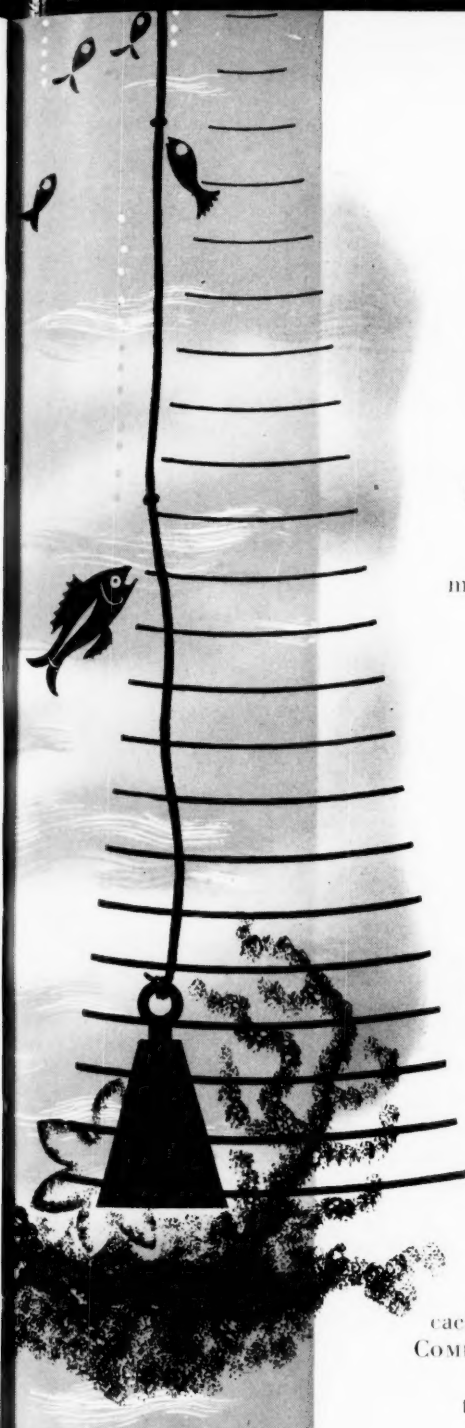

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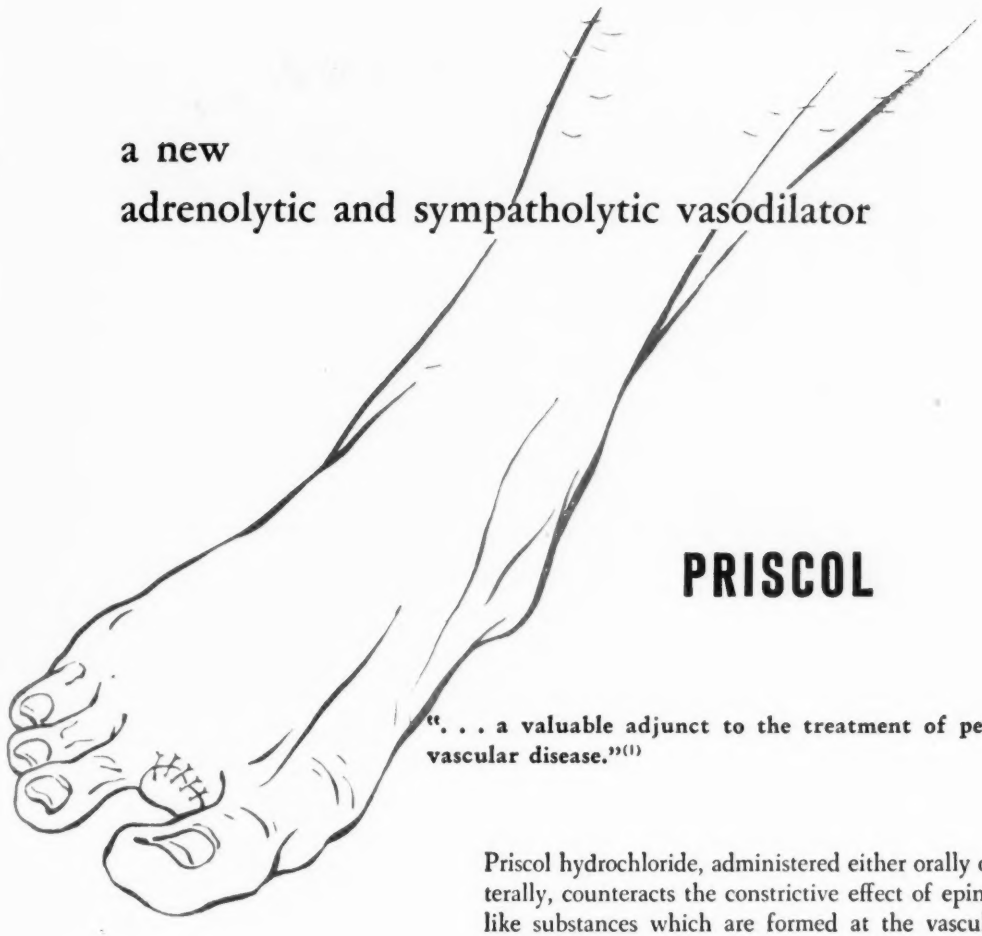

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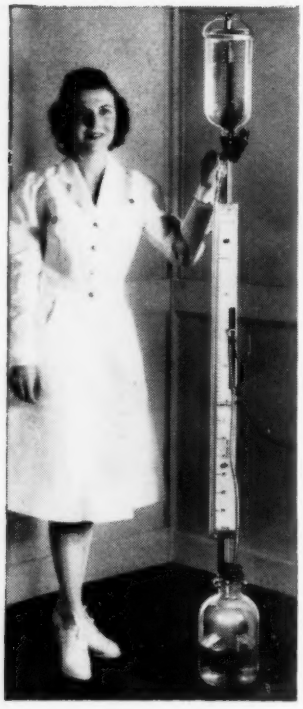

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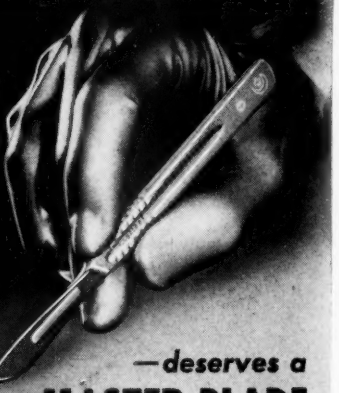

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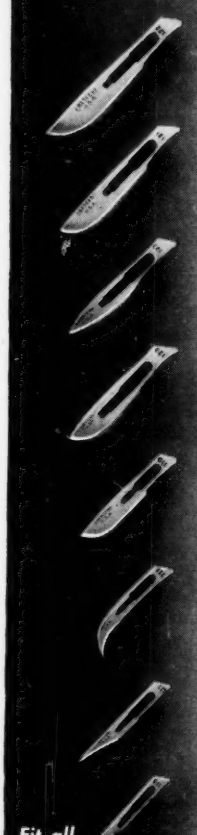

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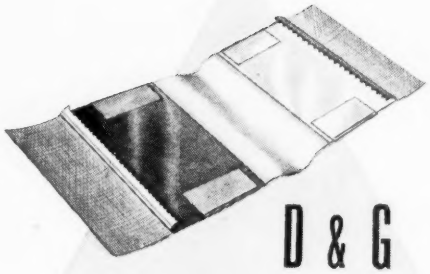

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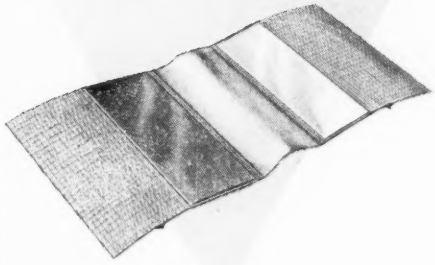

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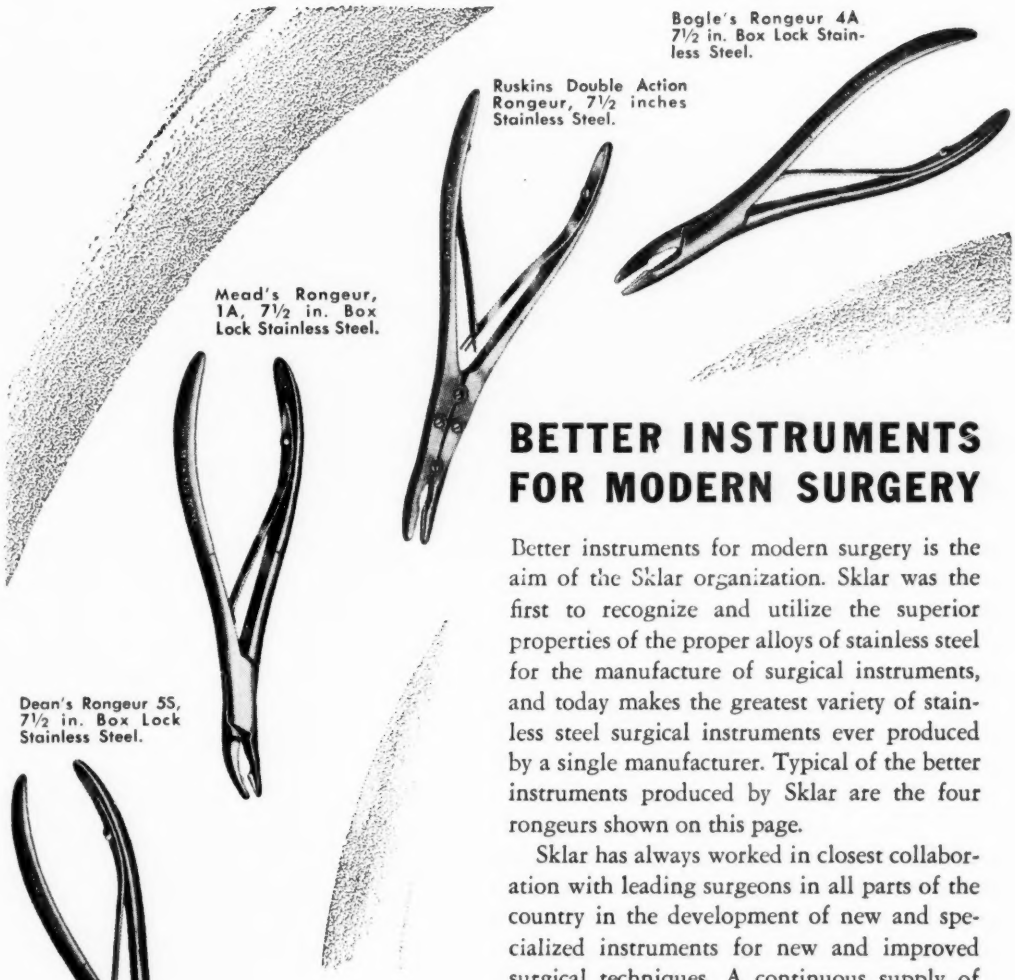

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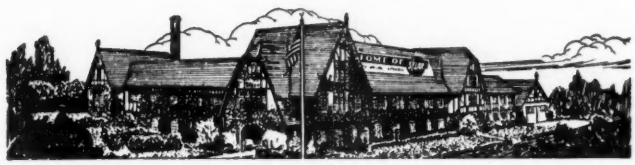

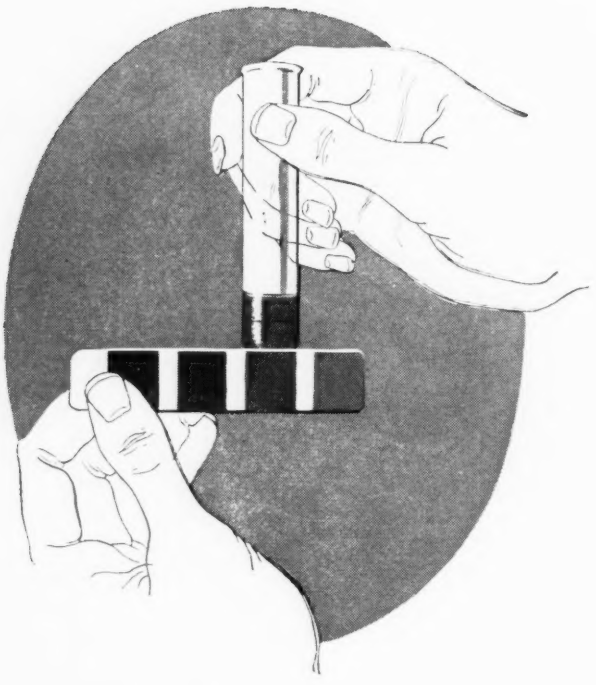

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VOL. 24 SEPTEMBER, 1948 NO. 3

Original Communications

Society for Vascular Surgery

VENOUS THROMBOSIS

ALTON OCHSNER, M.D., NEW ORLEANS, LA.

(From the Departments of Surgery, School of Medicine, Tulane University of Louisiana and the Ochsner Clinic)

IT IS with some trepidation that I speak on venous thrombosis before this assembly, because I am well aware of the splendid fundamental investigations in this field which have been conducted by many of the members of this organization. The contributions of Homans,[1-3] Allen and associates,[4-6] Bancroft,[7] de Takats and Fowler,[8, 9] and many others have added much to the present-day knowledge of this distressing, frequently dangerous, and usually disabling condition. Fortunately, at the present time because of a more thorough understanding of the underlying pathologic condition in venous thrombosis, much can be accomplished in preventing the occurrence of intravascular clotting and in treating the condition rationally once it has developed.

TYPES

Although there are some who will not agree with us, we are convinced from our experimental and clinical observations that in order to understand venous thrombosis correctly and to treat it rationally and satisfactorily, it is necessary to differentiate two types of thrombosis, thrombophlebitis and phlebothrombosis, which are alike only in the respect that in both the lumen of the vein contains a clot. These two types of venous thrombosis differ in etiology, pathology, clinical manifestations, prognosis, and therapy. Unless distinction is made between the two types, the therapeutic results are likely to be unsuccessful. Thrombophlebitis, as the name implies, is a condition in which there is inflammation of the venous wall associated with an intravascular clot, whereas phlebothrombosis is characterized by an intravenous clot unassociated with an inflammatory process in the venous wall. The presence of the inflammatory process in thrombophlebitis and its absence in phlebothrombosis is of great prognostic and therapeutic significance.

Presidential address delivered at the first annual meeting of the Society for Vascular Surgery, Atlantic City, N. J., June 8, 1947.

The clotting in thrombophlebitis is a result of injury to the vascular endothelium from mechanical trauma, invasion of the perivenous lymphatics by bacteria or their toxins, or chemical injury; whereas in phlebothrombosis, the intravascular thrombus is due to alterations in the cellular and fluid constituents of the blood which increase the clotting tendency, and to venous stasis. In thrombophlebitis the clot resulting from injury to the endothelium is firmly attached to the wall of the vessel and does not become detached except in the presence of suppuration; for this reason there is little or no danger of embolism. Moreover, because of the inflammatory process in the venous wall, impulses originate in the vein which are carried over the sympathetic nervous system to the ipsilateral arterioles, resulting in profound arteriolar spasm and edema, which may persist and cause prolonged disability. On the other hand, in phlebothrombosis without inflammation of the vein the clot is a coagulation thrombus, is only loosely attached to the venous wall, and can be detached easily with the development of embolism. It is recognized that if for any reason the clot in phlebothrombosis does not become detached, a superimposed inflammation of the venous wall may occur, the inflammatory reaction being secondary to the venous clot. Barker and associates[10] believe that this is the usual course of events and there is little or no danger of the clot becoming detached. Whereas this undoubtedly does occur in the exceptional case in which the clot does not become detached, it is hazardous to assume that the occurrence of embolism is not likely in phlebothrombosis. Greenstein[11] has shown conclusively in post-mortem examinations of persons dying from various causes that phlebothrombosis occurs in a high percentage of instances. Of 100 post-mortem examinations, thrombosis of the posterior tibial veins and muscular tributaries was observed in fifty-one and evidence of phlebitis was noted in only four of these. In the remainder there was no evidence of an inflammatory reaction in or around the vein. Also because of the lack of inflammatory reaction of the vein early in the course of phlebothrombosis, there is no arteriolar spasm and for this reason there are few if any symptoms. Because of the ease with which emboli can be detached in spite of absent or minimal symptoms, phlebothrombosis is potentially a fatal lesion. On the other hand, thrombophlebitis, even though the symptoms are severe, seldom endangers life although disabling sequelae are likely to persist for months, years, or even the remainder of the patient's life.

ETIOLOGY

Although venous clotting is more prevalent in certain persons (thrombosers), injury to body tissues, such as operative, obstetrical, or accidental trauma, or destruction of tissue by invasion of neoplastic disease or infection, is the principal predisposing etiologic factor. The precipitating factor is stasis in the venous circulation, which is responsible for the formation of the thrombi in the lower extremities. Circulatory retardation may be generalized, as in the elderly patient with cardiovascular disease, but is maximal in the venous channels of the legs and feet when the patient is confined to bed. On the other hand, phlebothrombosis exceptionally can occur in persons who are not bed-

ridden. McCutchen and Cantey[12] reported four cases of apparently normal persons in whom phlebothrombosis developed even though they were up and about and presumably well. The youngest patient was 48 and the oldest 62 years. Although the increased clotting tendency occurs in the blood of the entire body, it is well known that phlebothrombosis occurs primarily in the vessels of the lower extremity. Investigations of Neumann,[13] Rössle,[14] von Seemen,[15] Hunter and associates,[16] and Greenstein[11] demonstrated that thromboses begin in the veins which drain the calf muscles. Rössle[14] observed thrombosis of the calf vein in 25 per cent of routine post-mortem examinations. Hunter, Krygier, Kennedy, and Sneeden[16] reported that 52.7 per cent of 351 routine post-mortem examinations disclosed thromboses of the veins of the legs. Greenstein[11] noted thrombosis of the veins of both legs in all his cases. Posterior tibial veins and tributaries to the calf muscles were principally affected. In no instance were the femoral veins involved without concomitant thrombosis of the posterior tibial veins. The greater predilection of thrombosis for the deep veins of the leg is probably due to maximal stasis in those vessels. A patient lying quietly in bed, although moving the upper extremities more or less constantly, is likely to keep the lower extremities immobile. Since active muscular contraction is a prominent factor in the movement of blood in the veins of the extremities, complete relaxation of the muscles of the lower extremities, particularly those of the calf, causes stases of blood in the veins of these areas. Increased intra-abdominal tension from the use of tight abdominal bandages for gaseous distention of the intestines can compress the vena cava and increases the venous pressure in the veins of the lower extremity, which promote vascular stasis. Another factor favoring venous stasis is hypopnea. Venous circulation is improved by negative intrathoracic pressure, and if respiration becomes shallow as the result of an operative procedure, particularly laparotomy, the aspirating effect of negative pressure is reduced.

CLINICAL MANIFESTATIONS

The clinical manifestations of thrombophlebitis and phlebothrombosis vary considerably. Because of the inflammatory process involving the venous wall, the symptoms in thrombophlebitis are severe. We have demonstrated both experimentally[17] and clinically[18-20] that although the inflammatory lesion is in the vein, and this is particularly true when the femoro-iliac veins are involved, the symptoms are the result of spasm of the ipsilateral arterioles because impulses originating in the involved vein are carried over the sympathetic nervous system to the arterioles. Symptoms of thrombophlebitis are fever, pain, coldness, whiteness, and swelling of the extremity. The fever is undoubtedly the result of the inflammatory process involving the venous wall. The other manifestations are the result of ischemia caused by arteriolar spasm. Until relatively recently the significance of the whiteness and coldness of the extremity in phlegmasia alba dolens was not appreciated. That these two manifestations are the result of vasoconstriction can be demonstrated easily by their disappearance following vasodilatation. The symptoms and signs in thrombophlebitis, if the condition is not adequately treated, are likely to persist with the

production of disabling sequelae, such as persistent postphlebitic edema, postphlebitic ulceration, postphlebitic varicosities, and recurrent erysipeloid infections. In the relatively rare case of suppurative thrombophlebitis which occurs in the pelvic veins following criminal abortion, the symptoms are alarming and consist principally of chills and fever. The patient is critically ill and is apt to die unless adequate therapy is instituted promptly. Because of suppuration the intravenous clot becomes liquified and detached with the production of septic emboli resulting in infarction in the lung and even septicemia. Suppurative thrombophlebitis can occur in other parts of the body as well.

In contrast to the severe clinical manifestations associated with thromophlebitis, phlebothrombosis is accompanied by few or no manifestations. There may be slight elevation of temperature in a patient who is otherwise progressing satisfactorily; this has been described by Lautre[21] as "the little kick." Even more important than transitory elevation of temperature is elevation of the pulse rate, which is usually out of proportion to any elevation of temperature. This has been described as the "stepladder" pulse. Occasionally the patient complains of apprehension, which is unexplainable, and he may have a sense of impending disaster. With few exceptions the erythrocytic sedimentation rate is increased.

DIAGNOSIS

Although the diagnosis of thrombophlebitis is not difficult to make because the patient has severe symptoms and usually complains bitterly, the diagnosis of phlebothrombosis is usually made only by careful examination of the patient. It is a rule on our service to examine carefully the calves and feet of all patients past 40 years of age who have had any tissue injury and who are confined to bed. In this way it is possible to detect phlebothrombosis before symptoms appear. Compression of the calf or foot in phlebothrombosis is painful and upon forceful dorsal flexion of the foot pain in the calf and popliteal area is produced (Homan's sign).

Moses[22] has described a sign which he believes is more reliable than others in making a diagnosis of phlebothrombosis. In order to distinguish inflammatory lesions of the skin and subcutaneous lesions of the back of the leg from phlebothrombosis, he suggests that after the presence of tenderness has been determined by applying pressure anteriorly against the calf, pressure be exerted from side to side; if this causes no pain, the lesion may be diagnosed as phlebothrombosis, provided peripheral neuritis has been excluded by careful neurologic examination.

PROGNOSIS

As has already been emphasized, the prognosis in the two types of venous thrombosis also differs. Although the patient with thrombophlebitis has severe symptoms, is extremely uncomfortable, and is likely to have persistent disabling sequelae unless adequate therapy is instituted relatively early in the course of the disease, there is little or no danger to life with the exception of the unusual case of suppurative thrombophlebitis. On the other hand, the patient with phlebothrombosis who has few or no manifestations and who does not

appear ill may have massive pulmonary embolism resulting fatally. It is because of this latter possibility that a fatal outcome in the patient with phlebothrombosis is a potentiality.

TREATMENT

The treatment of phlebothrombosis is primarily prophylactic. Atraumatic surgical technique should be employed as much as possible in order to produce minimal tissue damage. The use of sharp dissection, the avoidance of massive ligation, and the employment of fine nonabsorbable suture material such as cotton are desirable. By decreasing the amount of tissue damage, the clotting tendency is minimized. On the other hand, in any patient who has had any tissue damage as a result of trauma or because of invasion by neoplastic disease or infection, it is imperative to prevent those factors which produce circulatory stasis and measures should be instituted to accelerate the return flow of blood from the lower extremities. This is particularly true in older persons with cardiovascular disease for whom bed rest is necessary. Active mobilization of the lower extremities by forcefully contracting the muscles against resistance, especially those of the calf, deep breathing, and increasing the flow of blood through the arterioles by the application of heat to the body will minimize stasis in the veins of the lower extremities. The application of compression bandages to the lower extremity to obliterate superficial veins will accelerate the blood flow through the deep veins. Early ambulation, which implies not only permitting the patient to get out of bed but also to walk, decreases venous stasis. If the patient gives a history of having had previous thrombosis, the use of anticoagulants is probably justified; in fact, it is our belief that the principal indication for their use is as a prophylactic measure in patients with a clotting tendency. Reich, Yhar, and Eggers[23] advocated the prophylactic use of dicumarol postoperatively. Bauer[24] did not recommend giving heparin before there is evidence of thrombosis. Dennis[25] has used dicumarol prophylactically in the surgical treatment of ulcerative colitis; of twenty patients subjected to operation, only three did not receive dicumarol preoperatively and all three died of pulmonary embolism. Bancroft[26] recommended the use of sodium thiosulfate, 10 c.c. of a 10 per cent solution intravenously for three days preoperatively, because the anticoagulant effect of heparin is dependent upon its sulfur content.

The curative treatment of thrombophlebitis consists of vasodilatation secured by anesthetization of the regional sympathetic ganglia with procaine hydrochloride. Since these patients are usually too sick to be placed in the prone position, the injection is generally done in the lateral decubitus position. The technique of injection is not difficult. Points two fingerbreadths lateral to the spinous processes of the first, second, third, and fourth lumbar vertebrae are chosen. A cutaneous wheal is made at each of these points with a long fine lumbar puncture needle (20 gauge, 13.5 to 15 cm. in length). The needle is introduced perpendicularly to the skin until it impinges against the transverse process. This latter structure serves as a landmark, because whereas there may be considerable difference in the thickness of the subcutaneous fat and the sacrospinalis muscle of a large, obese, muscular man and a little, thin woman, there is not much difference in the thicknesses of the bodies of their vertebrae.

After the transverse process has been identified, the direction of the needle is changed slightly either above or below and the needle is introduced for an additional two fingerbreadths. The point of the needle then lies in the retroperitoneal space on the anterolateral surface of the body of the vertebra where the lumbar sympathetic chain is located. Through each one of the four ports, 5 c.c. of 1 per cent solution of procaine hydrochloride is injected, so that the area in which the sympathetic nerves are located is flooded. This procedure is repeated daily as long as the patient has fever because although the pharmacologic effect of procaine hydrochloride lasts only two hours, the physiologic effect of anesthetization of the sympathetic ganglia is considerably longer than this.

Almost immediately following the injection there is complete relief of pain, the extremity becomes warm and loses its white discoloration, the temperature rapidly drops to normal, and the swelling begins to subside. With few exceptions the patient is well and able to be up within a week or ten days. In the patient with suppurative thrombophlebitis, it is imperative that radical therapy be used early in order to prevent detachment of the infected emboli with production of septic infarction of the lung and possibly septicemia. In order to accomplish this the vein proximal to the site of involvement is ligated or the involved vein is extirpated. If the pelvic veins draining the uterus are involved, ligation of the vena cava just above the bifurcation with simultaneous ligation of the two ovarian veins is the only rational procedure. Whereas previously the prognosis of thrombophlebitis was grave, the immediate institution of radical therapy before fatal septicemia has developed now provides extremely satisfactory results.

The treatment of phlebothrombosis is also radical. Although the symptoms are minimal or absent, a fatal outcome in these patients is a potentiality. Because the thrombus is not attached to the venous wall, it is imperative that either thrombectomy be done or the vein be ligated above the site of the thrombus. It is our belief that this procedure should take precedence over every other operative procedure except measures to combat massive hemorrhage. Ligation is accomplished with the patient in the head-up position in order to increase the venous pressure in the lower extremity and decrease the possibility of detachment of the clot during the operation. Under local analgesia a longitudinal incision is made over the femoral vein. The femoral artery is retracted and the vein exposed. Ligatures are loosely placed around the profunda, saphenous, and femoral veins above and below the profunda but they are not tied. A transverse incision is made in the superficial femoral vein distal to the junction of the profunda femoris. If a clot is present in the vein, there will be no free bleeding. A glass suction tube is introduced proximally and gentle suction maintained until the clot proximal to the opening of the vein is removed. This is followed by a free flow of blood from the vein proximally. After the vein has been ligated above the opening, as much of the clot as possible distal to the opening is removed. Since the profunda femoris is seldom involved, only the superficial femoral is ligated and divided. The procedure should be done bilaterally because it has been our experience, as well as that of others, that if the lesion has occurred on one side, it is likely to occur on the

opposite side. Greenstein[11] observed that venous thrombosis was bilateral in every instance in which post-mortem examination was performed. Compression bandages are applied to the extremity and the patient is instructed to mobilize the extremity as much as possible. He is gotten out of bed the following day.

REFERENCES

1. Homans, J.: Venous Thrombosis in the Lower Limbs: its Relationship to Pulmonary Embolism, Am. J. Surg. **38**: 316-326, 1937.
2. Homans, J.: Deep Quiet Venous Thrombosis in Lower Limbs; Preferred Levels for Interruptions of Veins, Iliac Sector or Ligation, Surg., Gynec. & Obst. **79**: 70-82, 1944.
3. Homans, J.: Medical Progress; Diseases of Veins, New England J. Med. **235**: 163-167, 193-198, 1946.
4. Allen, A. W.: Interruption of the Deep Veins of Lower Extremities in Prevention and Treatment of Thrombosis and Embolism, Surg., Gynec. & Obst. **84**: 519-527, 1947.
5. Allen, A. W.: Thrombosis and Embolism; Preliminary Report on Comparative Results of Femoral Vein Interruption and Dicumarol Therapy, Bull. New York Acad. Med. **22**: 169-184, 1946.
6. Allen, A. W., Linton, R. R., and Donaldson, G. A.: Venous Thrombosis and Pulmonary Embolism: Further Experience With Thrombectomy and Femoral Vein Interruption, J. A. M. A. **128**: 397-403, 1945.
7. Bancroft, F. W.: Proximal Ligation and Thrombectomy for Phlebothrombosis of Femoral and Iliac Veins, Ann. Surg. **121**: 175-184, 1945.
8. De Takats, G.: Effect of Sulfur Compounds on Blood Clotting, SURGERY **14**: 661-668, 1943.
9. De Takats, G., and Fowler, E. F.: The Problem of Thrombo-embolism, SURGERY **17**: 153-177, 1945.
10. Barker, N. W., Cromer, H. E., Hurn, M., and Waugh, J. M.: The Use of Dicumarol in the Prevention of Postoperative Thrombosis and Embolism With Special Reference to Dosage and Safe Administration, SURGERY **17**: 207-217, 1945.
11. Greenstein, J.: Thrombosis and Pulmonary Embolism, South African M. J. **19**: 350, 377, 1945.
12. McCutchen, G. T., and Cantey, W. C.: Phlebothrombosis Occurring in Absence of Trauma or Bed Rest, J. South Carolina M. A. **44**: 37-40, 1948.
13. Neumann, R.: Ursprungszentum und Entwicklungsformen der Bein-Thrombose, Virchows Arch. f. path. Anat. **301**: 708-735, 1938.
14. Rössle, R.: Ueber die Bedeutung und die Entstehung der Wadenvenenthrombo en, Virchows Arch. f. path. Anat. **300**: 180-189, 1937.
15. Von Seemen, H.: Operation und Gewebeschonung, Bezeihungen Zwischen Operationswunde und Entstehung, Vermeidung und Bekamphung der mittelbaren operationschadigungen (spontane Venethrombose und Pneumonie), Deutsche Ztschr. f. Chir. **223**: 85-129, 1930.
16. Hunter, W. C., Krygier, J. J., Kennedy, J. C., and Sneeden, V. D.: Etiology and Prevention of Thrombosis of the Deep leg Veins; a Study of 400 Cases, SURGERY **17**: 178-190, 1945.
17. DeBakey, M., Burch, G. E., and Ochsner, A.: Effect of Chemical Irritation of Venous Segment on Peripheral Pulse Volume, Proc. Soc. Exper. Biol. & Med. **41**: 585-590, 1939.
18. Ochsner, A., and DeBakey, M.: Thrombophlebitis; Role of Vasospasm in the Production of the Clinical Manifestations, J. A. M. A. **114**: 117-124, 1940.
19. Ochsner, A., and DeBakey, M.: Therapy of Phlebothrombosis and Thrombophlebitis, Arch. Surg. **40**: 208-231, 1940.
20. Ochsner, A., and DeBakey, M.: The Role of Vasospasm in Thrombophlebitis and its Treatment by Novocain Block of the Sympathetics, Tri-State M. J. **13**: 2654, 1941.
21. Lautre, M. A.: Watching for the Little Kick, South African M. J. **19**: 335-338, 1945.
22. Moses, W. R.: Early Diagnosis of Phlebothrombosis, New England J. Med. **234**: 288-291, 1946.
23. Reich, C., Yhar, M., and Eggers, C.: Dicumarol in Prevention of Postoperative Thrombosis and Pulmonary Embolism, SURGERY **18**: 238-243, 1945.
24. Bauer, G.: Heparin Therapy in Acute Deep Venous Thrombosis, J. A. M. A. **131**: 196-203, 1946.
25. Dennis, Clarence: Evaluation of Anticoagulant Therapy in Deep Venous Thrombosis of the Lower Extremities, Minnesota Med. **31**: 37-39, 1948.
26. Bancroft, F. W.: Review of Various Methods Used in Treatment of Phlebothrombosis of Extremities, New York State J. Med. **46**: 299-305, 1946.

POSTTHROMBOTIC SYNDROME OF THE LOWER EXTREMITY

Treatment by Interruption of the Superficial Femoral Vein and Ligation and Stripping of the Long and Short Saphenous Veins

Robert R. Linton, M.D., and Irad B. Hardy, Jr., M.D., Boston, Mass.

(From the Peripheral Vascular Clinic at the Massachusetts General Hospital)

DEEP venous thrombosis of the lower extremity involving the femoral and iliac veins produces permanent morphologic changes in the limb that affect the physiology of the venous circulation. This abnormal physiopathology results in the gradual development of a characteristic syndrome, climaxed usually after several years by a chronic indolent ulceration of the lower leg. The most common thrombotic sequelae of this syndrome are pain, edema, varicose veins, induration of the subcutaneous tissues above the internal malleolus, pigmentation, a chronic dermatitis of the skin of the lower leg, and chronic ulceration. They develop usually in this order over a period of four to five years after the thrombosis, but occasionally an ulceration may appear within one or two years and sometimes fifteen or twenty years may elapse before it develops. Homans[11] was the first to differentiate between simple varicose ulcers and the so-called postphlebitic ulcer. Since his report in 1917, numerous methods for the cure of this condition have been described but none is successful in all cases. The various types of ointments and local applications including iontophoresis that have been recommended are too numerous to recount. Needless to say the multiplicity of them indicates the ineffectiveness of all of them. Thompson[18] believed fungus infection of the feet to play an important etiologic role in the chronic ulcerations and advised eradication of mycotic foci. This form of therapy may aid in controlling the dermatitis but rarely if ever produces a permanent cure. The most noteworthy of the nonsurgical forms of treatment is the application of the paste type of boot, first described by Unna[21] in 1896, and the more recent modification utilizing an elastic adhesive bandage first reported by Wright[22] in 1930. This form of therapy frequently heals the ulcer but it does not cure it since it invariably recurs after discontinuance of the support.

Homans[11] in 1917 was the first to propose the radical excision of the ulcer and the surrounding pathologic skin and subcutaneous tissues including the deep fascia, with the application immediately of a split-thickness skin graft over the denuded area. Similar procedures, some more extensive than others, have been described by Mayo,[16] Trout,[20] Brown and associates,[5] Pennoyer,[17] and Douglas.[8] The purpose of this type of treatment was to excise the diseased tissues in the lower part of the leg rather than to correct the abnormal physiology of the venous circulation in the postthrombotic extremity. A more physiologic

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and less disfiguring operation was devised by one of us (R. R. L.),[14, 15] in which the communicating veins between the deep and superficial systems were interrupted and also the saphenous veins in the lower leg were removed. The rationale of this procedure was to remove the main varicosities of the lower leg and at the same time divide the communications between the deep and superficial systems of veins so that the increased pressure in the former would not be transmitted directly to the latter. Lumbar sympathectomy has been utilized in our clinic in a number of cases but unless it is combined with some other form of surgical treatment it has not cured the ulcerations.

The results obtained in a series of patients treated at the Massachusetts General Hospital by a number of these methods are shown in Table I. The ineffectiveness of them in many of the cases is apparent and for that reason a new type of surgical treatment consisting of interruption of the superficial femoral vein and ligation and stripping of the long and short saphenous veins has been developed, the results of which to date appear very encouraging. Buxton and his co-workers[6] in 1944 and Buxton and Coller[7] in 1945 were the first to report interruption of the femoral vein as a method of treating postthrombotic ulcerations. Homans[12, 13] in 1945 and 1946 recommended the interruption of the saphenous and the femoral veins in the postthrombotic extremity which shows marked venous congestion. Much credit should go to him because, although his publications were not the first, he has insisted for a number of years that the canalized postthrombotic vein is a useless structure and should be interrupted. These reports and the fact that in our clinic interruption of the femoral vein for deep venous thrombosis in over 3,000 extremities has seemed to prevent the development of the thrombotic sequelae including ulceration were sufficient stimulus to combine interruption of the superficial femoral vein with the complete removal of the long saphenous and the short saphenous vein also when it is varicosed. This form of therapy is directed at improving the physiology of the venous circulation in the postthrombotic extremity rather than attempting to cure the ulcer by local measures. In order that the rationale of this treatment may be better understood a short review of the pathologic physiology in the postthrombotic extremity is given.

TABLE I. RESULTS OF TREATMENT OF POSTTHROMBOTIC ULCERATIONS BY VARIOUS SURGICAL METHODS AT THE MASSACHUSETTS GENERAL HOSPITAL

METHOD	NUMBER OF EXTREMITIES			
	HEALED	PER CENT	UNHEALED	PER CENT
1. Skin graft alone	0	0	5	100
2. Injections alone	0	0	2	100
3. Excision of ulcer with primary skin graft	3	23	10	77
4. Ligation and division of saphenous vein	10	50	10	50
5. Lumbar sympathectomy	4	50	4	50
6. Ligation and division of communicating veins in the lower leg	27	55	22	45
Total	44	45	53	55

Blalock[4] has demonstrated that the oxygen content of the venous blood from a limb with varicose veins is not diminished. Holling, Beecher, and Linton[10] confirmed this observation and also showed the same to be true even in the presence of chronic postthrombotic ulcerations. As a result of these findings it is believed that hypo-oxygenation of the blood is not an etiologic factor in the thrombotic sequelae. There are two significant facts, however, concerning the postthrombotic syndrome that should be emphasized since an understanding of them aids in explaining at least some of the etiologic factors involved. First, it is believed that the thrombotic sequelae with the exception of pain and edema do not appear immediately but only after the deep veins have become canalized. Second, all postthrombotic ulcerations, unless they are extremely large, can be healed temporarily by placing the patient in bed with the leg elevated slightly above the heart level. In support of the first observation, the operative findings in 84 postthrombotic extremities reported in this article revealed that the femoral vein had become canalized in all instances. An analysis of 32 extremities with ulceration (Fig. 1) reveals that there was a period of from one to twenty-nine years after the venous thrombosis before the ulcer appeared. The majority, or 62 per cent, developed within ten years, and only 4, or 12.5 per cent, at the end of the first year. There will be those who doubt canalization can take place within one year, but it has been observed by one of us (R. R. L.) in a patient who also developed an ulceration within that period. Interruption of the canalized superficial femoral vein in this extremity produced rapid healing and it has remained healed for sixteen months without other therapy. The experimental work of Edwards and Edwards[9] and Beecher[2] also tended to corroborate this observation. The former have demonstrated that after a vein canalizes following phlebothrombosis the venous valves in it are incompetent. Beecher[2] has demonstrated a sustained high pressure in the saphenous vein with incompetent valves during muscular activity, whereas with a normal competent valvular system exercise reduces the venous pressure. A comparable situation, even more so, undoubtedly exists in the postthrombotic extremity in which the valves of the deep and the communicating veins also are incompetent. The pressure in the veins under these conditions is far above the colloid osmotic pressure of the blood, resulting in an increased quantity of lymph formation, as demonstrated by Beecher, Field, and Krogh.[3] In a normal leg the lymphatics would be sufficiently adequate to drain off this increased amount of tissue fluid, but as the result of the previous phlebitis the lymphatics have been damaged so that they do not function normally in the postthrombotic states. Holling, Beecher, and Linton[10] have correlated the increased edema formation with the high sustained venous pressure seen in these patients. Chronic lymphedema is practically universal in all cases and undoubtedly plays a role in the formation and chronicity of the ulcerations.

The induration seen in the tissues of the inner side of the lower leg the direct forerunner of the ulceration, it is believed also is secondary to the increased venous pressure. This condition has been designated by one of us (R. R. L.) as stasis cellulitis. The brown pigmentation of the skin of the lower

leg that ultimately appears is due to capillary hemorrhages secondary also to the increased venous pressure. The most marked changes in the skin and subcutaneous tissues and the most common site of ulcerations are on the inner side of the lower part of the leg just above the internal malleolus. It is believed that this is because the communicating veins in this region become incompetent from dilatation, since they pass out through tendons and are not supported by the muscles as are the ones higher in the leg. The varicose veins of the long

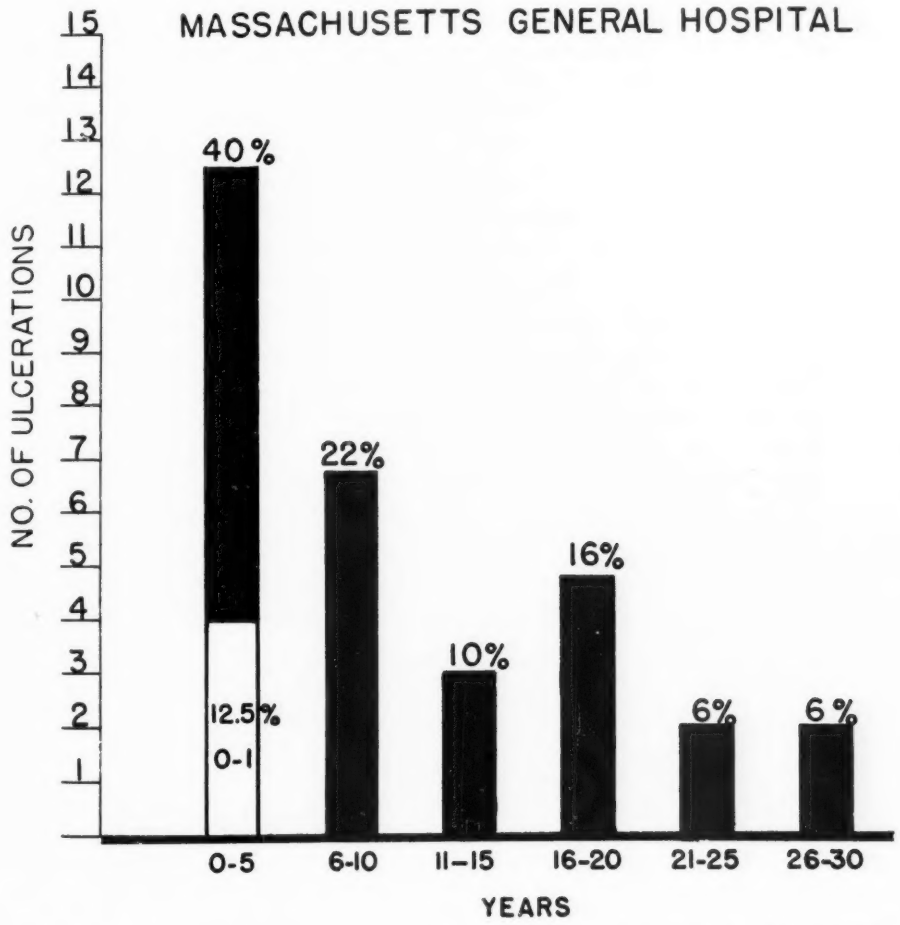

Fig. 1.—Years elapsed between venous thrombosis and ulceration in 32 postthrombotic extremities.

and short saphenous systems are most marked in the lower leg below the knee. They gradually develop over a period of years secondary to the increased venous pressure to which they are exposed after the deep veins have canalized and the communicating veins have become incompetent. The second observation, that bed rest with elevation of the extremity heals the ulceration, is confirmatory evidence of these facts, since by this means the venous pressure is greatly diminished and the lymphedema reduced, thus re-establishing a more normal

venous and lymphatic circulation. In summary, it is therefore believed that the thrombotic sequelae develop as a result of the sustained increased pressure in the veins of the lower extremity and the associated lymphedema.

Experience has revealed that interruption of the femoral vein alone, if ulcerations and varicosities are present, will not suffice to heal the former. These early experiences with poor results from femoral vein interruption alone necessitated the development of an operation, which in addition includes the proximal interruption of the long and short saphenous veins, and the stripping of them from the groin and popliteal space, respectively, to the ankle level. It is believed that the removal of these superficial veins if ulcers overlie them is extremely important, since the ulcerations have persisted in a few cases when the vein was not completely removed.

The selection of the patients for this type of surgical treatment is based primarily on the physical examination rather than on a history of a pre-existing deep venous thrombosis, since such a history cannot be obtained from all the patients. The most important part of the physical examination, to determine the advisability of performing the operation, is to ascertain the competency of the venous valves of the deep, communicating and superficial systems of veins. This is done by carrying out the so-called Trendelenburg test. The veins are emptied first of blood by elevating the extremity. A rubber tourniquet is applied to the leg just distal to the knee sufficiently tight to occlude only the superficial veins. The patient then stands up and if the veins below the tourniquet fill within a few seconds it demonstrates incompetent valves of the deep and communicating systems of veins. This observation is sufficient evidence to indicate the desirability of interrupting the superficial femoral vein. Since the dilated superficial veins on the inner side of the lower leg are either the long saphenous vein or its tributaries, removal of the main saphenous trunk from the groin to just below the internal malleolus is indicated also in these extremities. The demonstration of these superficial varicosities in some cases may be difficult due to the extensive fibrosis of the subcutaneous tissues, but chronic skin changes or ulcerations always indicate their presence. Similar conditions on the posterolateral surface of the lower part of the leg and the region of the external malleolus are considered sufficient reason to remove the short saphenous vein. From the experience gained by the study of these cases reported here, it is believed that the varicosed saphenous veins rarely if ever constitute collateral channels necessary for the return of blood from the extremity.

METHOD OF TREATMENT

Many of the patients with the postthrombotic syndrome when first seen come for treatment because of a chronic ulceration of the lower leg. It is necessary to heal this before operating on the extremity because of the danger of postoperative infection. For this reason when an ulceration is present the treatment is divided into three phases, preoperative, operative, and postoperative. If it is healed or an ulcer has not yet developed, of course the first one may be omitted.

Preoperative.—The preoperative treatment as a rule is carried out without hospitalization. This is important in these days since hospital beds are saved

for more acute cases and in addition the expense to the patient is reduced by a considerable amount. A bland ointment, such as boric acid, is applied to the ulcer. A generous gauze dressing is placed over it. The leg is wrapped with a gauze bandage so that there are several layers of it over the skin from the base of the toes to 3 cm. below the knee. This is covered next with a tight elastic adhesive bandage, making sure to cover the heel completely, and extending it above the gauze bandage, so that the upper portion of the elastic adhesive is applied directly to the skin. This latter point is important, as it keeps the entire dressing in place and prevents it from slipping down. The purpose of the gauze bandage is to prevent maceration of the skin as seen so frequently if the elastic adhesive is applied directly to it over the entire surface of the leg. These dressings are changed weekly at first and later at two-week intervals. As a rule it is possible to heal the ulcer within four to six weeks. After hospital admission a few days are taken to cleanse the skin thoroughly prior to operation. If the ulceration is too large for this type of treatment, it has been found advantageous to admit the patient to the hospital. There he is placed in bed with the leg elevated. Moist normal saline or boric acid solution dressings are applied at four-hour intervals. The base of the ulcer develops clean granulations usually within a week under this regime. Then a split-thickness skin graft is applied to the ulcer area. After another period of seven to ten days when the graft has taken sufficiently well the main operation on the veins can be carried out. Penicillin is given during the pre- and postoperative periods.

Operative.—Ether anesthesia has been used routinely. The superficial femoral and the long saphenous veins are exposed through a vertical longitudinal groin incision placed directly over and parallel to the femoral artery pulsations (Fig. 2). The femoral artery and vein are intimately bound together by perivascular scar tissue, the result of the previous venous thrombosis. Great care must be taken not to injure the artery in dissecting it free from the vein. It never should be completely isolated and retracted with a rubber tubing, since this may produce arterial thrombosis with gangrene of the lower part of the leg. The superficial femoral vein is isolated for about 3 cm. distal to the profunda femoris branch, which is always carefully visualized to be sure that the common femoral vein has not been isolated. Interruption of the latter and the saphenous vein may produce serious postoperative edema from which the extremity slowly if ever recovers. Venous pressures are taken in the superficial femoral vein by cannulating it with a needle attached to a manometer filled with normal saline solution (Fig. 3). The initial pressure is recorded a second reading is taken after the superficial femoral vein has been occluded temporarily, and finally a third one is taken with both it and the saphenous vein occluded. These pressures are taken as a precautionary measure to ascertain the effect of occluding both of these vessels, since occasionally it is found that the pressure rises to an alarming level. A rule has been established that if the pressure rises above 30 cm. after both the veins have been occluded, the stripping is not done until a later date because extensive bleeding may occur from the unligated

saphenous vein tributaries. More adequate collateral venous channels soon develop with a reduction in the venous pressure so that the stripping may be carried out safely. If a thickened canalized femoral vein is encountered, venous pressures rarely increase more than a few centimeters (Table II), indicating that an excellent venous collateral circulation has already developed. The femoral vein is divided immediately distal to the profunda femoris branch. Each

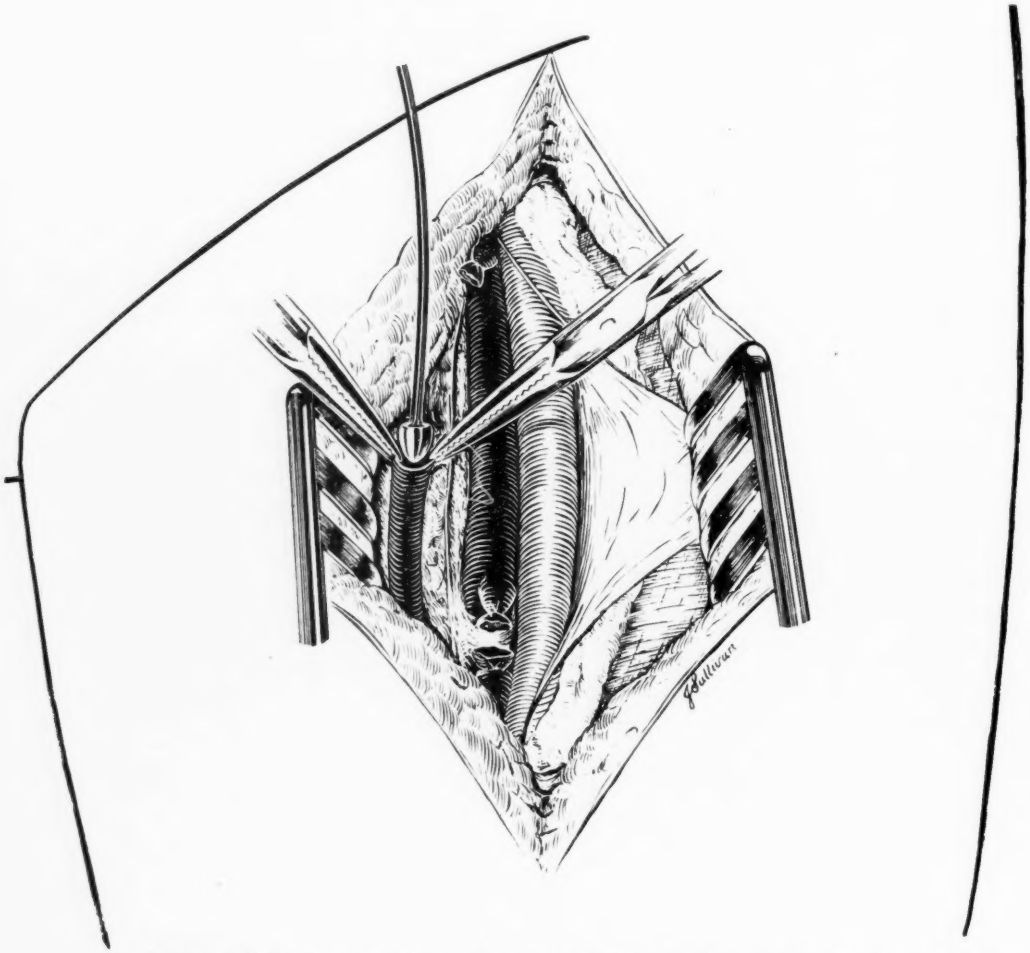

Fig. 2.—An artist's drawing showing exposure of long saphenous and superficial femoral veins. Note especially that the incision is parallel and over the femoral vessels. The superficial femoral vein has been ligated and divided distal to the profunda femoris and the saphenous vein at the saphenofemoral junction. The vein stripper is being inserted into the distal end of the saphenous vein.

end is ligated with a ligature and a transfixion ligature of silk or cotton. The patient is then placed in Trendelenburg position in order to reduce the venous pressure in the extremity and the main saphenous trunk is stripped from the groin to just below the internal malleolus after being interrupted at the saphenofemoral junction. An intraluminal type of stripper is used, similar to the one first described by Babcock[1] (Fig. 4). In some cases it passes readily from the groin to the ankle; in others it may be necessary to isolate the saphe-

nous vein just below the internal malleolus and pass the stripper upward to complete the removal of the entire trunk. The most important part of the saphenous vein to be removed is that which underlies the ulcer, since the poor results in these cases have been in those where the stripping was only carried just proximal to the ulcer area. The incisions are carefully sutured without drainage after completion of the stripping. The negligible amount of bleeding from the saphenous tributaries in these cases is always surprising in view of the fact that both the femoral and the saphenous veins have been interrupted. If the short saphenous vein is varicosed or if there are chronic skin changes or an ulceration in the region of the lateral malleolus, it should be stripped also from

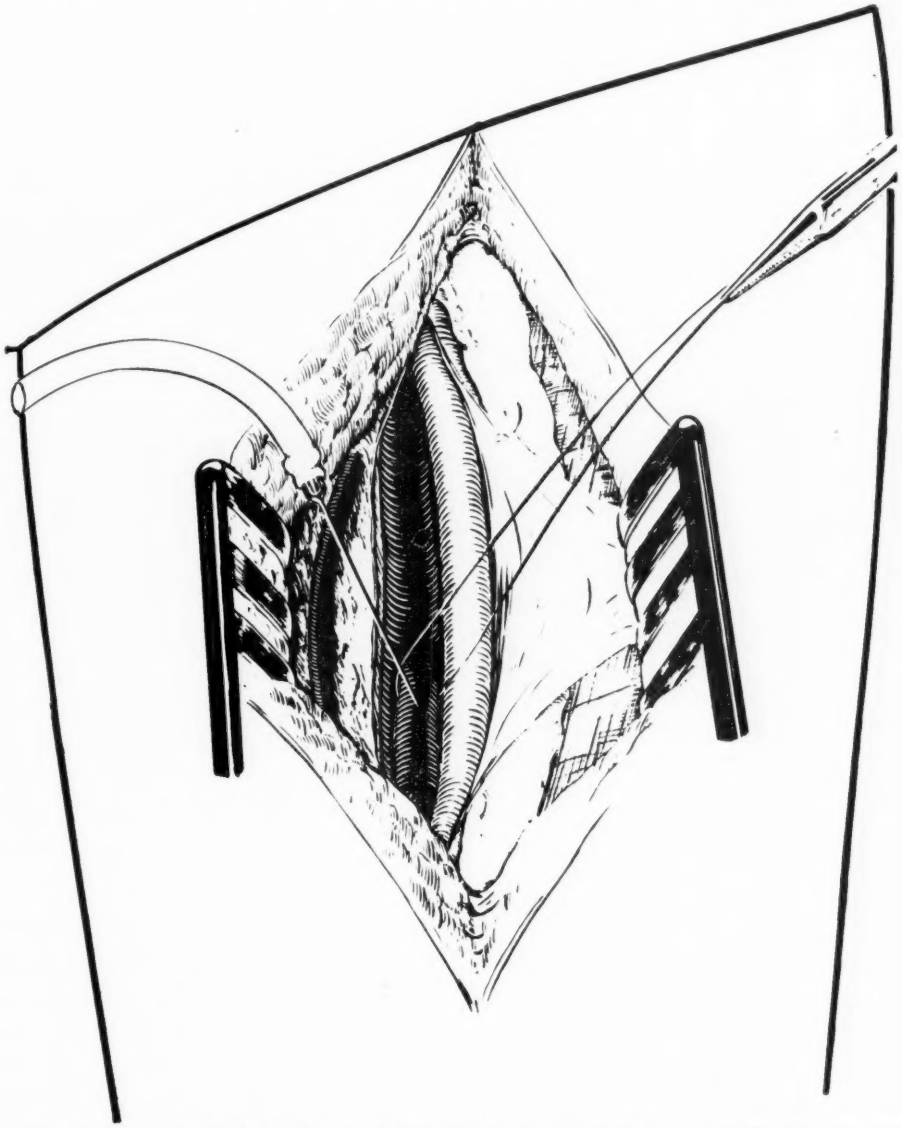

Fig. 3.—An artist's drawing showing method of cannulating superficial femoral vein to obtain venous pressures. These are recorded before and after occluding it, and again with the saphenous vein also occluded.

TABLE II. VENOUS PRESSURES IN FEMORAL VEIN OF THIRTY POSTTHROMBOTIC EXTREMITIES, MASSACHUSETTS GENERAL HOSPITAL

CASE NO.	INITIAL FEMORAL VEIN PRESSURE*	AFTER OCCLUSION OF SUPERFICIAL FEMORAL VEIN*	AFTER OCCLUSION OF SUPERFICIAL FEMORAL AND LONG SAPHENOUS VEINS*
1	3.5	16.0	19.0
2	4.0	6.5	16.5
3	4.0	15.5	24.0
4	4.5	7.0	7.0
5	6.0	8.0	8.5
6	6.0	21.0	21.0
7	6.0	20.0	20.0
8	6.0	15.0	22.5
9	6.0	9.0	10.0
10	7.0	12.0	14.0
11	7.0	28.0	44.0
12	7.0	12.5	16.0
13	7.5	14.5	14.5
14	7.5	12.5	14.5
15	8.0	8.5	8.5
16	8.5	14.5	14.0
17	8.5	9.0	9.0
18	10.0	19.0	23.0
19	11.0	11.5	15.0
20	11.0	16.5	19.0
21	11.5	12.0	14.0
22	12.5	32.5	45.0
23	12.5	19.5	22.0
24	13.5	14.0	15.0
25	13.5	14.5	13.5
26	14.0	18.0	18.0
27	16.0	17.5	17.5
28	17.0	20.0	24.0
29	20.0	21.0	24.0
30	20.0	20.0	45.0
Lowest	3.5	6.5	9.5
Highest	20.0	32.5	45.0
Mean	9.5	15.5	19.0

*In centimeters of normal saline solution.

the popliteal space to a point distal to the lateral malleolus. The patient is turned in the prone position on the operating table in order to facilitate this part of the operation. The vein is isolated through a transverse incision in the popliteal space. Again every effort is made to remove the entire trunk. After closure of all the incisions, a gauze roll 5 to 6 cm. in diameter is placed over the course of the long saphenous vein (Fig. 5) and the extremity bound from the toes to the groin with two four-inch width elastic bandages.

Postoperative.—Penicillin, twenty-five thousand units, are administered intramuscularly every three hours for five days. The foot of the bed is elevated on shock blocks for twenty-four hours. The patient is allowed to be ambulant on the first or second postoperative day. The skin sutures are removed on the fifth postoperative day, and as a rule the patient is discharged from the hospital on the seventh to the tenth day with instructions to wear an elastic bandage from the toes to the knee during the day. Regular check-ups are made at two-week intervals at first and then monthly for the first three months. A small

injection of a sclerosing solution may be necessary to eradicate a large varix that is still present in some instances. A varying degree of lymphedema is often seen and in such cases the patient is instructed to wear an elastic bandage or stocking until this disappears.

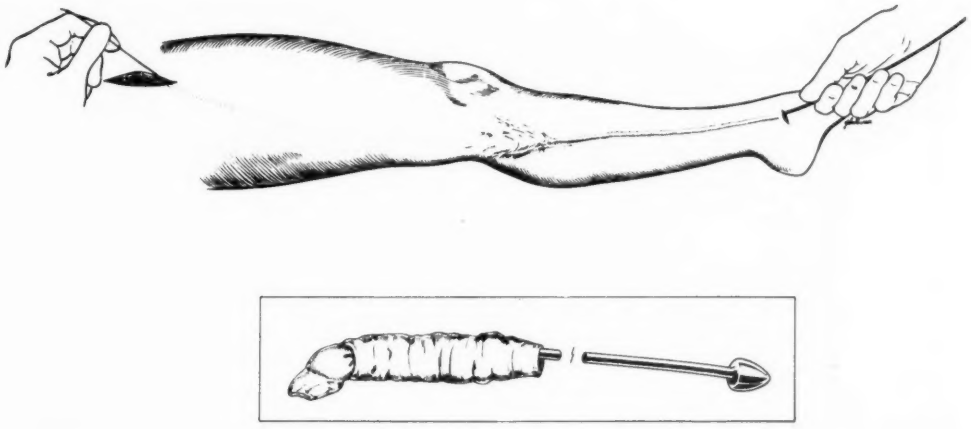

Fig. 4.—An artist's drawing showing the intraluminal type of stripper in the saphenous vein. The inset shows the vein telescoped on the stripper. When it is removed in this manner the vein seldom breaks; if it does another incision is frequently necessary to complete the removal of the vein.

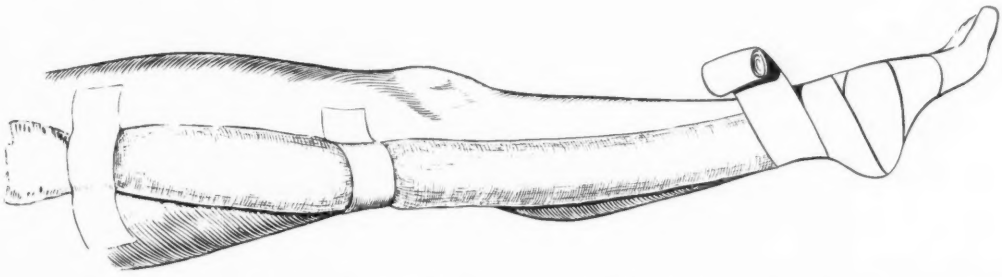

Fig. 5.—An artist's drawing showing the gauze roll fastened to the extremity over the course of the long saphenous vein. An elastic bandage is wound around it and the extremity for hemostasis. Both are removed after forty-eight hours.

DISCUSSION

This report is based on 49 patients who presented thrombotic sequelae in one or both lower extremities. There were 31, or 63 per cent, females and 18, or 37 per cent, males. The age distribution reveals that 34, or 70 per cent, were between 40 and 60 years of age. The youngest was 24 years and the oldest 69 years of age (Table III). The chief complaints of these patients when first seen were chronic indolent ulcer in 25, or 50 per cent; varicose veins in 14, or 30 per cent; swelling of the extremity in 7, or 14 per cent; and "phlebitis" in 3, or 6 per cent. A definite history of a pre-existing deep venous thrombosis of the lower extremities was given by 46, or 94 per cent, of the patients and in 3 it was not obtained. It had occurred bilaterally in 23, or 47 per cent, of the

TABLE III. AGE IN DECADES AND SEX OF PATIENTS WITH POSTTHROMBOTIC SYNDROME, MASSACHUSETTS GENERAL HOSPITAL

AGE (YR.)	MALES	FEMALES	TOTAL	PER CENT	
21 to 30	1	1	2	4	
31 to 40	4	5	9	18	
41 to 50	6	15	21	42	70%
51 to 60	4	9	13	28	
61 to 70	3	1	4	8	
	18 (37%)	31 (63%)	49	100	

Youngest, 24 years; oldest, 69 years.

patients and unilaterally in 26, or 55 per cent. Physical examination and operative findings revealed a higher incidence of pre-existing deep venous thrombosis than was indicated by the history (Table IV). Postthrombotic changes in the extremities were observed bilaterally in 35, or 71 per cent, of the patients and unilaterally in 14, or 29 per cent, making a total of 84, or 100 per cent, of the extremities. This higher incidence was confirmed also at operation since a perivascular postthrombotic cicatrix and sclerosis of the femoral vein (Fig. 6) were observed in 70, or 83 per cent, of the extremities and unilaterally in 14, or 17 per cent, making a total of 84, or 100 per cent, of the extremities. The pre-existing deep venous thrombosis followed surgical conditions in 20 patients, parturition in 16, medical diseases in 8. It occurred spontaneously in 2 and in 3 no history was obtainable.

TABLE IV. PRE-EXISTING DEEP VENOUS THROMBOSIS IN POSTTHROMBOTIC SYNDROME, MASSACHUSETTS GENERAL HOSPITAL

BASED ON	HISTORY				PHYSICAL EXAMINATION				OPERATIVE FINDINGS			
	PATIENTS		EXTREMITIES		PATIENTS		EXTREMITIES		PATIENTS		EXTREMITIES	
	NO.	PER CENT	NO.	PER CENT	NO.	PER CENT	NO.	PER CENT	NO.	PER CENT	NO.	PER CENT
Bilateral with	20	41	40	64	35	71	70	83	35	71	70	83
Bilateral without	3	6	6									
Unilateral	26	53	26	28	14	29	14	17	14	29	14	17
Total	49		72		49		84		49		84	

The most common signs and symptoms in the order of their frequency seen in these 84 extremities with the postthrombotic syndrome were lymphedema in 84, or 100 per cent; pigmentation in 80, or 95 per cent; varicose veins in 79, or 94 per cent; pain in 54, or 64 per cent; stasis dermatitis in 49, or 59 per cent; stasis cellulitis in 48, or 57 per cent; ulcerations in 36, or 43 per cent. Of the latter 21 were still open when the patient was admitted to the hospital, 7 were healed but gave a history of repeated recurrences in the past, and 8 had been healed before the patient's admission to the hospital with elastic pressure bandages. All except 2 of the open ones were healed with bed rest, elevation of the extremity, moist dressings, and intramuscular injections of penicillin, so that the skin was in a satisfactory condition for surgery within seven to ten days. The two unhealed ones were covered with split-thickness skin grafts before proceeding with the operation on the veins.

Lymphedema was not only the most common sequela occurring in all the extremities but it had persisted for the longest period since it developed concomitant with the venous thrombosis. The other sequelae developed at varying intervals in the postthrombotic period. It is interesting to note that there was a great difference in the time of appearance of the ulcerations in the various patients. They developed at the end of a year in 4 of them, whereas in two

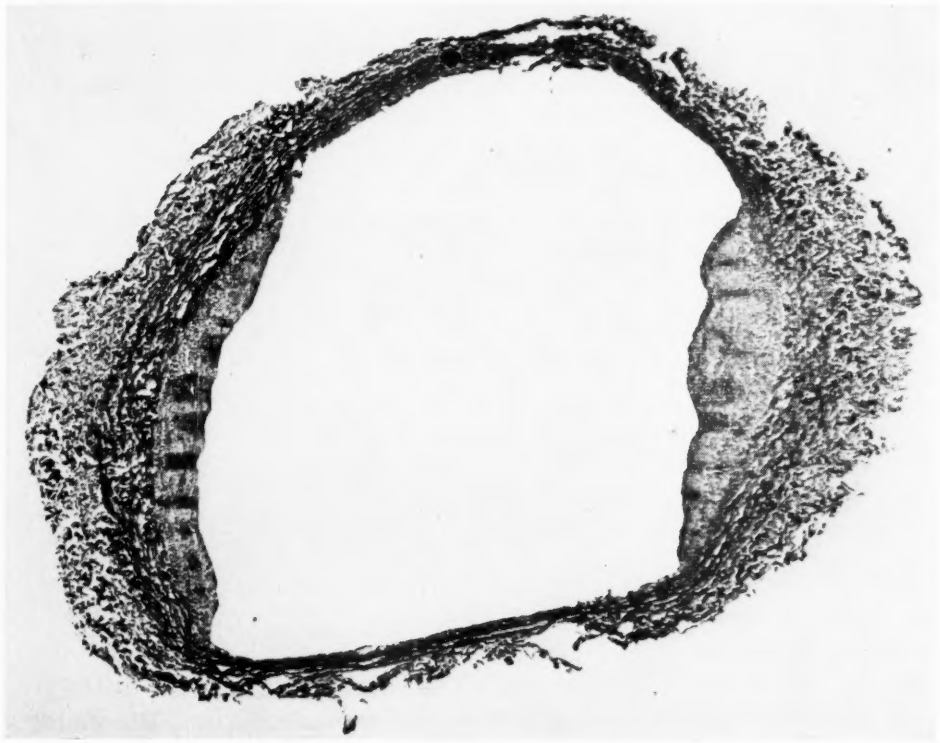

Fig. 6.—An enlargement of a microphotograph of a canalized postthrombotic femoral vein. Note the marked thickening of the vein wall with fibrous tissue.

cases twenty-nine years elapsed between the venous thrombosis and the occurrence of the ulceration. The majority of them, 62 per cent (Fig. 1), appeared within ten years. The explanation is not obvious for the great variation in this time of appearance nor the fact that less than one-half of the extremities were ulcerated. Local injury undoubtedly plays a role but can hardly be the entire answer.

The surgical treatment performed on 84 postthrombotic extremities consisted of the interruption of the femoral vein just distal to the profunda femoris, the ligation of the long saphenous vein at the saphenofemoral junction and the removal of it from the groin to the ankle by a stripping process, and in addition the short saphenous vein when it was found varicosed. It is important that the common femoral vein should not be interrupted, since this along with the saphenous vein interruption would shut off too much of the venous return.

The rationale of this method of treatment, it is believed, is that the venous blood is shunted into smaller deep veins which still have competent valves, thus possibly reducing the venous pressure especially during exercise; it prevents a direct reversal of the venous blood flow down the deep veins from the large venous reservoirs of the trunk when the erect position is assumed; it preserves the profunda femoris, the medial, and the lateral circumflex femoral veins as collateral channels for the return of the blood from the extremity; and it removes the main superficial varicosities.

Bilateral superficial femoral vein interruption and ligation with stripping of the long saphenous vein were performed on 35, or 71 per cent, of the patients; 14 had it done only on one leg (Table V.) Four of the patients had the stripping done as secondary procedures, 3 because of the recurrence of the

TABLE V. OPERATIVE PROCEDURES IN FORTY-NINE PATIENTS WITH POSTTHROMBOTIC SYNDROME, MASSACHUSETTS GENERAL HOSPITAL

OPERATION	PATIENTS NO.	PATIENTS PER CENT	EXTREMITIES NO.	EXTREMITIES PER CENT
Bilateral superficial femoral vein interruption, ligation & stripping of long saphenous vein	35	71	70	83
Unilateral superficial femoral vein interruption, ligation & stripping of long saphenous vein	14	29	14	17
Ligation & division of short saphenous vein	9	30	9	18
Ligation & stripping of short saphenous vein	6		6	
Skin graft to ulcer	2		2	

ulceration after femoral vein interruption alone, and the fourth because the femoral vein pressure rose to a level of 45 cm. after interruption, so the stripping was delayed for a week until the pressure had fallen to 24 cm. In the latter case it was feared that serious hemorrhage might occur from the tributaries of the saphenous vein with such a high venous pressure. Combining all these operative procedures there was a total of 84 extremities that had both the superficial femoral vein interrupted and the long saphenous vein ligated and stripped. The short saphenous vein was interrupted at the saphenopopliteal junction in 9 extremities and in addition stripped in 6 others. This made a total of 15 extremities in which this vein was interrupted. One patient who had a recurrent ulcer over the lateral malleolus showed an enlarged incompetent short saphenous vein which should have been removed, as it is believed the persistence of this vessel explained the recurrence of the ulceration.

Venous pressures were taken during the operation for two reasons in the superficial femoral vein before and after interrupting it and again with the long saphenous vein also occluded. First, these readings were taken to determine if either one or both of the vessels, especially the saphenous, were important collateral channels for the return of blood from the limb. The initial pressure varied considerably. The lowest was 3.5 cm. of normal saline solution and the highest was 20 cm.; the mean value was 9.5 centimeters. After occluding the superficial femoral vein the lowest value was 6.5 cm. the highest 32.5 cm., and the

mean 15.5 cm. With both this vessel and the long saphenous vein occluded the lowest pressure was 9.5 cm., the highest 45 cm., and the mean 19 cm. The readings obtained in 30 of the extremities are shown in Table II. An analysis of these proves that in the majority of postthrombotic extremities neither the superficial femoral nor the long saphenous vein, or both of them, is necessary for the return of blood from the limb. The second reason for determining the level of venous pressure in the extremity was in the event that it became so elevated that severe hemorrhage might occur following the stripping of the saphenous vein. The pressure in 4 instances with both vessels occluded rose to approximately 45 cm. In the first two there were no complications following the procedure, but extensive postoperative ecchymosis occurred in the third one, so that in the fourth case the stripping was postponed for one week when the pressure had dropped to 24 cm., a more nearly normal level.

The postoperative complications were few and not serious (Table VI). The most troublesome one was edema in 6 extremities, necessitating the use of an elastic support. The mortality rate was zero. At the present time it is our opinion that no extremity has been made worse by the operative procedure as described.

TABLE VI. POSTOPERATIVE COMPLICATIONS IN EIGHTY-FOUR POSTTHROMBOTIC EXTREMITIES, MASSACHUSETTS GENERAL HOSPITAL

COMPLICATIONS	NUMBER
Sepsis in groin incision	1
Hematoma in groin incision	1
Lymph collection in groin incision	1
Penicillin Dermatitis	2
Secondary anemia	1
Edema of extremity	6
Mortality rate	0

A number of the patients with persistent ulcerations had previous surgical procedures without benefit. These included 14 instances of interruption of the saphenous vein at the saphenofemoral junction with and without injection of sclerosing solutions; 1 with multiple ligations of the long saphenous vein; 3 lumbar sympathectomies, and 3 patients who had had interruption of the superficial femoral veins. The poor results obtained with these forms of therapy are not surprising in view of our past experiences (Table I). The fact that 3 did not do well after superficial femoral vein interruption alone over periods of twenty-two, fifteen, and twelve months is considered to be of significance, indicating the necessity of combining it with ligation and stripping of the saphenous veins. As a secondary procedure this has been carried out in these three cases with gratifying results to date for periods of two, eight, and eight months.

The follow-up statistics on the 84 postthrombotic extremities cover a period varying from one to sixteen months (Table VII). An analysis of the results revealed that pain was a symptom in 54, or 64 per cent, of the extremities. It was relieved in 34, or 63 per cent, and incompletely relieved in 20, or 37 per

TABLE VII. FOLLOW-UP STATISTICS ONE TO SIXTEEN MONTHS IN EIGHTY-FOUR POST-THROMBOTIC EXTREMITIES, MASSACHUSETTS GENERAL HOSPITAL

SEQUELA	PRESENT IN NO.	PRESENT IN PER CENT	RELIEVED IN NO.	RELIEVED IN PER CENT	STILL PRESENT IN NO.	STILL PRESENT IN PER CENT
Pain	54	64	34	63	20	37
Edema	84	100	38	45	46	55
Varicose veins	79	94	26	33	53	67*
Stasis cellulitis	48	57	18	37	30	63
Stasis dermatitis	49	58	36	73	13	27
Pigmentation	80	95	0	0	80	100
Ulcerations	36	43	29	80	7	20†

*Relieved with postoperative injections of sclerosing solution.

†One practically healed three months postoperatively; 2 recurred, healing with injections; 2 recurred, not healing; 2 were persistent, not healing.

cent. Edema was present in all and was relieved in 38, or 45 per cent, so that no elastic support had to be worn, whereas in 46, or 55 per cent, it was not completely relieved, necessitating the wearing of an elastic bandage or stocking. Many of these patients are improved and it is felt will ultimately be able to go without support. Some patients have worn such a protection for so long that it is difficult to get them to discard it. Varicose veins were demonstrable in 79, or 94 per cent, of the extremities. They disappeared after the operation in 26, or 33 per cent, and with a few injections of a sclerosing solution in the remaining 53, or 67 per cent, of the extremities have been relieved. Induration of the subcutaneous tissues or stasis cellulitis was present in 48, or 57 per cent. It was relieved in 18, or 37 per cent, and is still present but improved in the remaining 30, or 63 per cent. Stasis dermatitis observed in 49, or 58 per cent, was relieved in 36, or 73 per cent, and still present in 13, or 27 per cent. Pigmentation of the skin of the lower leg was the least affected of the thrombotic sequelae. It was observed in 80, or 95 per cent, and is still present in all of these extremities. There has been a slight improvement as the intensity of it seems to have diminished somewhat, but it is felt that it will never entirely disappear. Fortunately, it is the least troublesome of the sequelae from the patient's viewpoint. Ulcerations were present in 36, or 43 per cent, of the limbs. They were healed in 29, or 80 per cent, and 7, or 20 per cent, have not healed. In the latter group one was practically healed after 3 months, 2 had recurred and were temporarily healed again with injections of sclerosing solutions in the varicose veins feeding the ulcer areas, 2 recurred, and 2 have not yet healed.

The explanation for the failure to heal these 7 ulcerations is not entirely clear but the duration of the ulcers before the treatment was carried out may be a factor since in most of the long-standing cases a greater degree of local fault in the tissues beneath and surrounding them from fibrosis is usually found than in those of shorter duration. The mean age of the unhealed group of 7 was 9 years, whereas in the healed group of 29 it was 5.2 years. If four patients from the latter are subtracted in whom the duration of the ulcers was fifteen, sixteen, twenty-four, and thirty-nine years, it leaves 25 in whom the mean age

was only 2.3 years. Another factor in 3 of the unhealed ulcers, it is believed, was the fact that the saphenous veins were not removed from beneath the ulcer areas. It would appear, however, from these statistics that the earlier adequate surgical treatment is performed in the ulcer group the better is the chance of cure. It is realized, of course, that the follow-up period in the cases reported here is too short to claim a permanent cure by this method of a chronic condition which has baffled the medical profession for centuries, but nevertheless the results to date are sufficiently encouraging to warrant further trial.

CONCLUSIONS

1. Deep venous thrombosis of the lower extremity involving the femoral and iliac veins produces permanent morphologic changes in the extremity that result in a characteristic postthrombotic syndrome.

2. The postthrombotic syndrome is characterized by the following states which appear usually in this order: pain, edema, varicose veins, stasis cellulitis, stasis dermatitis, pigmentation, and chronic ulceration.

3. It is believed that the postthrombotic syndrome develops primarily as a result of a high sustained venous pressure in the extremity due to incompetent valves of the deep, communicating, and superficial systems of veins following canalization of the deep veins.

4. Interruption of the femoral vein distal to the profunda femoris branch, ligation and stripping of the long saphenous vein, and in addition the short saphenous vein if it is varicosed, have been performed in 84 extremities presenting the postthrombotic syndrome in various stages. The common femoral vein should not be interrupted and the importance of removing the entire main saphenous trunks is emphasized.

5. None of the extremities has been injured by the procedure, indicating that the superficial femoral and the saphenous veins are not necessary collateral venous channels in the postthrombotic extremity.

6. The postoperative complications have been few and not serious, and the mortality rate was zero.

7. The results of a follow-up study varying from one to sixteen months in 84 extremities subjected to this form of treatment are encouraging, but further years of observation are necessary to determine the true value of this method.

REFERENCES

1. Babcock, W. W.: A New Operation for the Extirpation of Varicose Veins of the Leg, N. York M. J. **86**: 153, 1907.
2. Beecher, H. K.: Adjustment of the Flow of Tissue Fluid in the Presence of Localized, Sustained High Venous Pressure as Found With Varices of the Great Saphenous System During Walking, J. Clin. Investigation **16**: 733, 1937.
3. Beecher, H. K., Field, M. E., and Krogh, A.: The Effect of Walking on the Venous Pressure at the Ankle, Skandinav. Arch. f. Physiol. **73**: 133, 1936.
4. Blalock, A.: Oxygen Content of Blood in Patients With Varicose Veins, Arch. Surg. **19**: 898, 1929.
5. Brown, J. P., Byars, L. T., and Blair, V. P.: A Study of Ulcerations of the Lower Extremity and Their Repair With Thick Split Skin Grafts, Surg., Gynec. & Obst. **63**: 331, 1936.
6. Buxton, R. W., Farris, J. M., Moyer, C. A., and Coller, F. A.: Surgical Treatment of Long-standing Deep Phlebitis of Leg: Preliminary Report, SURGERY **15**: 749, 1944.

7. Buxton, R. W., and Coller, F. A.: Surgical Treatment of Long-standing Deep Phlebitis of Leg: Supplementary Report, SURGERY **18**: 663, 1945.
8. Douglas, B.: Conservative and Radical Measures in the Treatment of Ulcer of the Leg, Surg., Gynec. & Obst. **61**: 458, 1935.
9. Edwards, E. A., and Edwards, J. E.: The Effect of Thrombophlebitis on the Venous Valve, Surg., Gynec. & Obst. **65**: 310, 1937.
10. Holling, H. E., Beecher, H. K., and Linton, R. R.: Study of the Tendency to Edema Formation Associated With Incompetence of the Valves of the Communicating Veins of the Leg. Oxygen Tension of the Blood Contained in Varicose Veins, J. Clin. Investigation **17**: 555, 1938.
11. Homans, J.: The Etiology and Treatment of Varicose Ulcers of the Leg, Surg., Gynec. & Obst. **24**: 300, 1917.
12. Homans, J.: The Surgery of the Veins of the Legs: Varicosity and Some Problems in Thrombosis, Rhode Island M. J. **28**: 565, 1945.
13. Homans, J.: The Late Results of Femoral Thrombophlebitis and Their Treatment, New England J. Med. **235**: 249, 1946.
14. Linton, R. R.: The Communicating Veins of the Lower Leg and the Operative Technic for Their Ligation, Ann. Surg. **107**: 582, 1938.
15. Linton, R. R., and Keeley, J. K.: The Postphlebitic Varicose Ulcer, Am. Heart J. **17**: 27, 1939.
16. Mayo, C.: Treatment of Varicose Veins, Surg., Gynec. & Obst. **2**: 385, 1906.
17. Pennoyer, G. P.: The Treatment of Varicose Ulcers and Veins, Ann. Surg. **99**: 997, 1934.
18. Thompson, K. W.: Studies on Relationship of Dermatomycosis to Ulceration and Gangrene of Extremities, Yale J. Biol. & Med. **16**: 665, 1944.
19. Trendelenburg, F.: Ueber die Unterbindung der Vena saphena magna beis Unterschenkelvaricen, Beitr. z. klin. Chir. **7**: 195, 1890-1891.
20. Trout, H. H.: Ulcers Due to Varicose Veins and Lymphatic Blockage, Arch. Surg. **18**: 2281, 1929.
21. Unna, P. G.: Ueber Paraplaste eine neue Form medikamentoser. Pflaster, Wein. med. Wchnschr. **46**: 1854, 1896.
22. Wright, A. D.: Treatment of Varicose Ulcers, Brit. M. J. **2**: 996, 1930.

THE SURGICAL TREATMENT OF ESSENTIAL HYPERTENSION

IV. Case Selection and Technique as Influencing Results

Geza de Takats, M.D., Ormand C. Julian, M.D., and
Edson F. Fowler, M.D., Chicago, Ill.

(From the Department of Surgery, University of Illinois College of Medicine)

THOUSANDS of operations have been performed to date for hypertension, but neither the classification and case selection nor the technique employed has been uniform. It is, therefore, difficult to compare the results of various clinics engaged in this work. In this communication we wish to present our classification, case selection, and the techniques employed as they influence results. This topic is obviously controversial and leaves room for a great deal of discussion.

CLASSIFICATION OF ESSENTIAL HYPERTENSION

The basis of all classifications is the concept of Keith, Wagener, and Barker[1] that hypertension per se causes increasing damage in cerebral, retinal, cardiac, and renal structures and that the stage of the disease can be defined by the advancing damage in these organs. In a previous report de Takats, Heyer, and Keeton[2] presented a table which was based on the combined data of Wagener and Keith, Palmer and Smithwick, and our own earlier experiences. As a weakness of all attempts at grading hypertension, one point became obvious: the degree of involvement in the brain, retina, heart, kidney, or peripheral vessels does not run a parallel course and a patient with a severe cerebrovascular accident can have surprisingly intact cardiac and renal function. For this reason, subsequent workers have used subdivisions of this classification. Peet and Isberg[3] used six groups. While their first and sixth groups are identical with Wagener and Keith's first and last (fourth) groups, they introduce a group of patients with early hypertension in whom symptoms predominate but who display no organic involvement except in the fundi, and another three groups in which cardiac, cerebrovascular, or renal disease are predominant. Smithwick[4] in his latest communication used twelve groups, determined by sex, age, and pulse pressure. Hinton and Lord[5] graded the severity of hypertension on the basis of four in each of the organs: brain, retina, heart, and kidney. A total count of more than eleven contraindicates operation.

Our group uses a simple classification in the three groups, which are essentially those of Wagener and Keith except that Group 1 is a combination of 1 and early 2 of Wagener and Keith and Group 3 is a combination of late grade III and IV of Keith and associates.[1] This classification arose out of our experience, that the malignant and premalignant phases of hypertension are not a surgical problem and second, that the grade I and early grade II hypertensives

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of Wagener and Keith can be grouped together since results of operation in this group are uniformly excellent. Accordingly, the three groups of essential hypertension are:

Group 1. Age below 40 years; minimal or no detectable organic damage; normal blood pressure on complete rest or barbiturates; casual diastolic pressures above 100 mm. Hg.

Group 2. Age from 20 to 55 years; moderate vascular sclerosis in all organs; well-demonstrable angiospasm; diastolic pressures cannot be lowered below 110 mm. Hg by any method; rising diastolic pressure during the course of last six months.

Group 3. Large recurrent retinal hemorrhages and exudates or papilledema; high fixed diastolic pressure, which cannot be lowered below 120 mm. Hg; congestive or anginal heart failure; poor renal function; numerous cerebrovascular accidents; an actual malignant or premalignant state of hypertension with continuous maximal angiospasm uninfluenced by either pressor or depressor stimuli.

All these classifications are simply the expressions of the degree of organic vascular damage. Another viewpoint, namely whether the hypertension is renal or nonrenal, does not find any expression in these gradings. Some authors[7] feel that the neurogenic hypertension is the ideal case for sympathectomy, whereas the renal group should be excluded from the operation. Two of us, in an article published recently,[8] came to the paradoxical conclusion that the renal group did better than the so-called neurogenic, especially since the neurogenic group turns out to be more and more a neuroendocrine state.

What is urgently needed is a separation of the renal from the nonrenal factor; it is becoming obvious that both may operate in the same patient, in varying sequence and varying proportions. Thus, an exciting neurogenic mechanism may produce repeated cortical ischemia in the kidney, as in the fascinating experiments of Trueta and his co-workers.[9] Conversely, a renal hypertension produced experimentally may enter a second neurogenic phase, as indicated by Ogden and his group.[10] For practical purposes, neither the depressor effect of spinal anesthesia nor that of the barbiturates has given a clear-cut answer. The use of monoethyl ammonium chloride (etamon), a sympathetic depressant, produces a rapid fall in blood pressure, in an animal with a Goldblatt clamp and also in one with the moderator nerves sectioned.

To complicate the picture further, the pituitary-cortico-adrenal mechanism has to be taken into consideration not only in the typical Cushing syndrome, but in many patients with hypertension in whom a neurogenic factor is obvious and whose general adaptive mechanism[11] is overstimulated.

The emotional element, the personality factor in patients with hypertension, has been the subject of extensive studies[12] and suffice it to say here that while treatment directed toward this factor has never been capable of definitely lowering blood pressure, the severity of the psychoneurotic element may contraindicate operation. In such patients, psychotherapy should precede and not follow surgical treatment, as borne out by some unfortunate personal experiences.

Looking at hypertension then from the standpoint of the surgeon, it must become clear to him that in the complex mechanism of hypertension he can influence some of the factors. These factors are depicted in the diagram (Fig. 1).

Splanchnic nerve section as practiced today varies in extent and we shall deal with these variations later. It can diminish sympathetic-adrenal activity, inhibit reflex renal spasm, and diminish general arteriolar tone. How much benefit occurs from inhibition of afferent impulses from the viscera is not sufficiently known, but the hypothalamus is readily activated from many outside stimuli. Certainly it does not affect the psyche, the parenchymal lesion in the kidney, and probably not the adrenal cortex, although some of our early work did suggest that lipid storage occurred there after splanchnic section.[13] Little is known about the late effects of splanchnic section on the adrenal cortex. From the standpoint of case selection, then, it is important not only to exclude patients with excessive vascular damage as manifested in the premalignant and malignant phase of hypertension, but also those in whom psychic, cortico-adrenal, or renal-parenchymal factors are predominant.

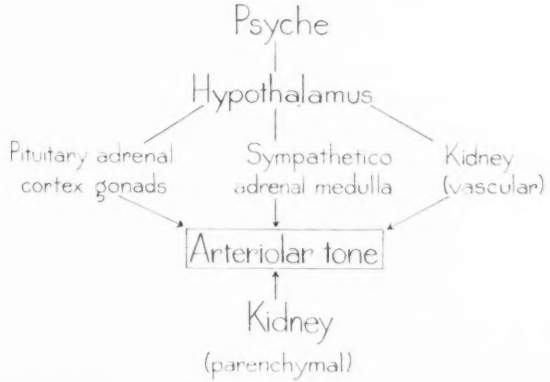

Fig. 1.—The mechanism of hypertension. Sympathectomy may interrupt the tract between the hypothalamus and the sympatheticoadrenal system. It may influence the vascular supply of the kidney.[9] In advanced parenchymal lesions of the kidney, it should not decrease the pressor substances entering the circulation. It is unknown, whether the corticoadrenal lipids which seem to be mobilized under stress (Selye[11]) are affected by splanchnic nerve section (see text).

CONTRAINDICATIONS TO OPERATION

These considerations, then, make our contraindications clear. The contraindications to splanchnic nerve section for essential hypertension can be summarized under four headings:

1. Extensive organic damage to brain, retina, heart, or kidney
2. Mechanical obstruction to circulation
3. Marked psychic involvement
4. Obvious pituitary-cortico-adrenal activity

1. Extensive organic damage to brain, retina, heart, or kidney. For us, persistent papilledema and nitrogenous retention are absolute contraindications. A previous stroke or coronary occlusion by themselves are not contraindications if the rest of the organs are satisfactory, but naturally influence prognosis.

2. Mechanical obstruction to the circulation, such as exists in aortic regurgitation, coarctation of the aorta, but also in the rigid, sclerotic aorta of all atheromatous patients with a high pulse pressure and a diastolic pressure stabi-

lized between 100 and 110 mm. of mercury. Arteriolar tone in these patients is not significantly increased.

3. Marked psychic involvement. Neither blood pressure nor mental attitude is improved after operation and surgery often aggravates the mental status in such patients.

4. Obvious pituitary-corticoadrenal activity, which in our present state of knowledge may be influenced only by radiation or possibly by a low sodium diet, but not by surgery. This may be measured by any of the tests used for the detection of corticoadrenal insufficiency except that deviation from the normal is on the side of hyperfunction. This group is often labeled neurogenic but neurohormonal or neuroendocrine is more appropriate. Recently through the work of Selye,[11] and Sayers and his associates,[14] it has become well established that under various types of stress, corticoadrenal cholesterol is emptied. The latter authors showed that according to the intensity and duration of pituitary stimulation and the time after which the adrenal gland is examined, five degrees of adrenal response may be recognized. In applying such experimental data to the subject of human hypertension, further studies are now in progress, which need not be discussed here. Suffice it to say, however, that corticoadrenal activity seems to be present in many forms of human hypertension,[15] and that this angle of the problem has been so far neglected, compared with the renal factor. It is to be stressed here that we are not discussing the full-blown picture of the Cushing syndrome[16] but a secondary corticoadrenal stimulation accompanying many forms of essential hypertension. I would predict that the emphasis which is on the renal factor today will shift in the next few years to the corticoadrenal factor.

VARIATIONS IN TECHNIQUE

There are many variations, extensions, and reductions in the extent of sympathetic denervation, but they may be crystallized around five basic patterns, which are presented in the accompanying diagram. Our apologies are due those who have used other modifications, but for the sake of simplifying the discussion, these five techniques have been depicted (Fig. 2). To carry this diagram up to date, we are relying on recent personal communications.

The technique of Adson and Craig removes through a retroperitoneal, subdiaphragmatic exposure the major splanchnic nerve from the diaphragm to and including the tip of the celiac ganglion, together with the two upper lumbar ganglia. The last available report of Adson and Allen on results obtained with this technique was made in 1940.[17] Craig,[18] in a personal communication, stated that he is now extending this operation to various supradiaphragmatic levels. The technique of Peet[19] which, according to his latest personal communication, is still the original supradiaphragmatic retropleural approach, done in one stage, removes the splanchnic nerve from the eighth dorsal segment to the diaphragm and the chain from the eighth to the twelfth dorsal segment, inclusive. Smithwick[20] combined the two approaches by a transdiaphragmatic route and removes the splanchnic nerve from the eighth dorsal segment to the celiac ganglion and the chain from the eighth dorsal segment to at least include

the first lumbar segment and often the second. He, too, has done high dorsal sympathectomies of late. Hinton[21] advocated a transpleural approach through the tenth rib, and he removes the splanchnic nerve from the fifth dorsal segment to the celiac ganglion, the chain from the third dorsal to the third lumbar segment. Grimson,[22] in his total sympathectomy, removed the entire splanchnic nerve and the sympathetic chain from the stellate ganglion to the fourth lumbar segment in two, three, and four stages.

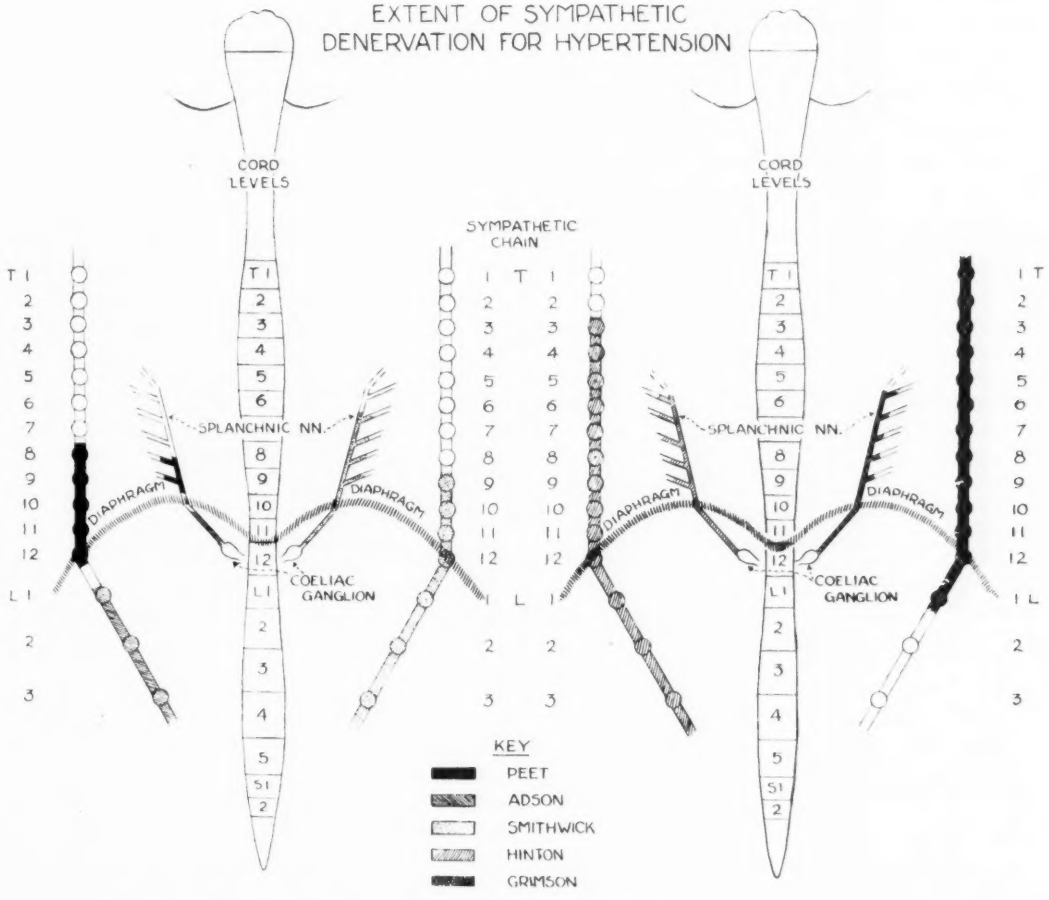

Fig. 2.—Extent for sympathetic denervation for hypertension. The approaches of Peet and Smithwick are extrapleural, those of Hinton and Grimson are transpleural. Quite recently Poppen described an extrapleural approach, with the extent of denervation used by Hinton. Drawing based on recent personal communications from these authors.

Obviously the mortality must rise with the extent of the operation and the acceptance of malignant or premalignant types of hypertension for operation.

Since 1940 we adopted the technique of Smithwick[23] and most of our present operations are based on his procedure except that the twelfth rib is not resected, but the eleventh is in its entirety, and that the two adjacent ribs are approximated with fine silver wire or No. 1 chromic catgut. The removal of the major splanchnic nerve from the mid-thoracic level to the tip of the celiac ganglion

and of the sympathetic chain from the ninth dorsal to the twelfth lumbar ganglion inclusive is considered the *minimal procedure*. Nothing less than this is considered sufficient and it is felt that the postural hypotension which results from the addition of the lumbar sympathectomy is an important part of the operation. An extension of this procedure to include the dorsal sympathetic chain to the third or second dorsal ganglion seems indicated, when the hypertensive damage is far advanced, when there is considerable cardiac damage or angina, but its disadvantages are also obvious. In the first place, the transthoracic approach through the tenth or the eighth rib carries a much higher morbidity than the retropleural approach; the number of pleural effusions, atelectases, and massive collapses is much greater. Second, such patients, especially if they have a tendency to sweat, perspire profusely in the neck and face and their heat-regulating mechanism is considerably upset. Third, the section of the cardiac accelerators, which run in part through the upper dorsal sympathetic ganglia, prevents the postural tachycardia or the tachycardia following lung collapse and thus decreases the minute volume of the heart. This may throw a perfectly capable heart, whose venous return has been markedly decreased by the splanchnic section, into failure, resulting in pulmonary edema. Such was the case in a 50-year-old army officer, in whom a bilateral transthoracic sympathectomy, with removal of the chain from the third dorsal to the first lumbar level on both sides resulted in an acute heart failure immediately after the second stage.

One of us (O. C. J.) has been performing the high transpleural sympathectomies, without gaining the impression that the results were any better, but recently we have become impressed with the suggestion of Poppen and Lemmon[24] who add the resection of the eighth rib to the eleventh and remove the sympathetic chain between the third or fourth dorsal to below the second lumbar segment retropleurally. If one were certain that the addition of the higher segments is essential, this might become our routine procedure, but not enough time has elapsed to warrant the adoption of this procedure except for experimental purposes.

POSTOPERATIVE COMPLICATIONS

Elsewhere two of us (E. F. F. and G. de T.) will report on postoperative complications in detail.

CARDIOVASCULAR ACCIDENTS

Cerebrovascular accidents were observed in three patients, two of whom had visual phenomena and one a full-blown cerebral thrombosis. *Coronary thrombosis* was seen in one patient and *coronary insufficiency* occurred in five. We have seen no postoperative uremia, possibly because of our practice of not operating on patients with less than 50 per cent of the normal urea clearance (20 c.c. of urea clearance per 100 c.c. of blood).

These are probably inavoidable sequelae in a group suffering from advanced cardiovascular disease.

PULMONARY COMPLICATIONS

Residual pneumothorax, atelectasis, and atelectatic pneumonia are predominantly dependent upon expert anesthesia which unfortunately is still not uniformly available. In most institutions, the director of anesthesia is fully trained and highly skilled, but the training program of anesthesiology has made an executive out of him with inexperienced residents actually administering intratracheal, positive-pressure anesthesias. This needs emphasis because our morbidity and mortality as observed in three separate series seems to depend mostly on the type of anesthesia the patient receives. Two deaths in 250 patients occurred on the operating table and were deaths from anesthesia.

Intercostal neuralgia, along the course of the resected eleventh rib, has been a real problem. Neither cutting, crushing, or injecting the nerve, nor leaving it intact or teasing it out with resection of the posterior root ganglion has seemed to make any difference. We have also tried paravertebral novocain injections and x-ray to the paravertebral ganglia with indifferent results. Distinct from this pain which radiates ventrally and caudally along the course of the nerve is a severe continuous back pain, somewhat relieved by a fracture board, which seems to be due to a muscular insufficiency of the back. The sacrospinalis muscle, this potent splint of the spinal column, loses some of its attachments to the lower ribs when it is dissected medially and retracted. Many patients have spinal arthritis which seems to flare up, having lost some of the splinting support. If the vertebral end of the rib is not resected and the long muscles of the back are as little disturbed as possible, this type of pain does not seem to occur as often.

Postural hypotension, postural dyspnea, and postural tachycardia are present with adequate denervation but are not disturbing after six to eight weeks. We have not found it necessary to prescribe elastic corsets and hose, but simply warn the patient not to rise suddenly and to keep moving. Shaving in front of a mirror in the standing position must be avoided for two months. Postural dyspnea is probably a mild coronary insufficiency due to poor venous return. Postural tachycardia is a useful compensatory mechanism to make up for the diminished stroke volumes which are demonstrable with the oscillometer. Its elimination by total sympathectomy has been demonstrated by Grimson[25] but we are not convinced that a slow pulse under these conditions is of any advantage.

The subject of sterility in the male has been recently studied by Poppen and Lemmon.[24] It is certain that many hypertensive patients are impotent prior to operation; it is also true that this question should not be discussed unless the patient himself brings it up. Otherwise a psychic inhibition is bound to complicate matters. One of us (G. de T.), with Helfrich,[26] has presented evidence that motile spermatozoa may be present after resection of the dorsolumbar chain and the splanchnic nerves.

Lately attention has been focused on the fact that the visceral sensory afferent fibers of the upper abdomen are sectioned by sympathectomy for hypertension so much so that one of us (G. de T.), with Walter,[27] has recently reported the performance of splanchnic nerve sections for intractable pancreatic pain.

Other reports indicate that painless perforations of the duodenum may occur,[28] or that reactivation of a gastric ulcer with massive hemorrhages can follow[29] splanchnic nerve section. We have not observed such a complication in this series and wish to emphasize that as soon as a peritoneal involvement occurs, somatic sensory stimulation would give danger signals. The increased gastroduodenal peristalsis which follows splanchnic section seems not to be experienced by the patients but lack of appetite or nausea at the smell of food may occur. Tincture of belladonna inhibiting the vagal preponderance eliminates such symptoms.

The mortality in this series was 2 in 250 patients, less than 1 per cent. As stated before, both patients died during the operation, obviously from bronchial obstruction. In the series of two institutions, there has been no mortality, whereas in the third institution the department of anesthesia is just being reorganized.

OUR RESULTS

This report is based on the study of 250 hypertensive patients who can be grouped as shown in Table I.

TABLE I. GROUPING OF PATIENTS OPERATED UPON, 1934 TO 1946

GROUP	NUMBER PATIENTS
1	55
2	171
3	24
Total	250

Of the 250 patients, 2 were lost as a result of anesthetic deaths on the operating table, which is our only mortality. None in Group 3 survived more than 1½ years. Out of the remaining patients, 202 are available for study. The operations were analyzed as resulting in failures, dubious benefit, marked benefit, and complete remission. *Failure* was recorded when the blood pressure returned shortly or within a year to the preoperative level and symptoms were uninfluenced. *Dubious benefit* was noted when the results were not clear-cut. Symptomatic relief was present, but neither heart size nor electrocardiogram improved and blood pressure was not markedly lowered. *Marked benefit* was registered, when the blood pressure was stabilized at a diastolic level between 100 and 110 mm. of mercury when symptoms subsided and working ability was restored. *Complete remission* of hypertension was recorded when blood pressure returned to below 140/90 mm. of mercury for at least one year, when symptoms subsided, and when earning power was fully restored.

Our results were recorded according to the groups of hypertension and the four types of results. Of the 202 patients analyzed, the 139 patients, or 69 per cent of the total had either a complete reduction of blood pressure to normal or showed marked benefit and were regarded as having successful results. The patients showing dubious benefit or failure were also lumped together making 63 patients, or 31 per cent of the total. Breaking them down into the three groups, the results were obtained as shown in Table II.

TABLE II. RESULTS OF SPLANCHNIC NERVE SECTION FOR ESSENTIAL HYPERTENSION IN 202 PATIENTS (FOLLOW-UP FROM ONE TO SIX YEARS)

GROUP	NUMBER CASES	SUCCESS (PER CENT)	FAILURE (PER CENT)
1	55	85	15
2	123	75	25
3	24	0	100
Total	202	69	31

THE ANALYSIS OF FAILURES

We have then 31 per cent failures, and the majority of these can be regarded as due to poor case selection. The results in all of the twenty-four patients belonging to our third group were failures and for several years now the patients with malignant and premalignant types of hypertension have been regarded as inoperable and refused operation. It should be mentioned that both Peet and Isberg[3] and Smithwick[20] record good results in cases of malignant hypertension, but it is our feeling that the malignant phase there was based alone on papilledema. We too have some startling results in a few patients with papilledema, but no corresponding vascular damage in retinal, cardiac, or renal vessels. Papilledema and high spinal fluid pressure per se do not place these patients in the inoperable group.

The analysis of failures indicates three reasons for the lack of success. Poor case selection has already been commented on. Insufficient denervation (less than the classic Smithwick procedure) seemed to be present in seven patients, and it was possible in three to improve the results by more extensive denervation. This was especially striking in one patient, in whom an infradiaphragmatic splanchnicectomy was done elsewhere, five years before, with not even a temporary reduction in pressure and in whom five years later a generous supradiaphragmatic resection resulted in marked benefit (grade II result).

In our first and second groups, there are nineteen patients, in whom shortly, or at least within one year, a recurrence or a dubious result was noted and of these the six failures noted in Group 1 are most important. These were young individuals with all the criteria of a vasospastic nonorganic arteriolar involvement, who were sufficiently denervated and yet showed a progressive arteriolar disease uninfluenced by operation.

TABLE III. ANALYSIS OF FAILURES IN SIXTY-THREE PATIENTS, 1940 TO 1946

GROUP	CASES NUMBER	CASES PER CENT OF TOTAL	REASON	
1	8	15	Insufficient denervation	2
			Unexplained	6
2	31	25	Insufficient denervation	5
			Heart failure	7
			Stroke	6
			Unexplained	13
3	24	100	Poor case selection	*

*The third group has been regarded as inoperable since 1942.

The causes for failure here are mostly speculative, although some suggestive data are accumulating. In the first place, it is possible that pleochromocytomas or cortical adrenal tumors have been overlooked. In the high transthoracic types of approach, this might be all the more possible since one cannot explore the subdiaphragmatic structures. Second, a corticoadrenal activity may well be the dominant factor in some hypertensions even without visible or palpable enlargement and it is not known that splanchnic section would influence such a process, which no doubt is mediated through the corticoadrenal hormone of the pituitary. Finally, we have seen and reported the case of one patient[8] who showed no reduction in blood pressure following splanchnic section, who died suddenly, two years after operation, at the age of 22 years, and in whom a complete autopsy revealed no anatomic cause for death or for the hypertension.

In our present state of knowledge, then, we must admit that a certain small group of patients, even although their organic damage is slight, does not respond to splanchnic nerve section and that future work will have to elucidate the mechanism of this type of hypertension. Such work is now in progress.

SUMMARY

A group of 250 patients have been followed for at least one year and not more than six, in whom the minimal procedure consisted of a total splanchnic nerve section with removal of the sympathetic chain above the ninth dorsal and below the second lumbar ganglia. More extensive procedures were tried in a selected group of patients but nothing can be said as yet about their being superior; the morbidity certainly rises with their use. The patients were grouped as being in an early, marked, and too advanced stage. For five years now none of the last group has been accepted. There were two anesthetic deaths in this series and no postoperative mortality. The results were excellent in the first, fair in the second, and poor in the third group. The possible role of a corticoadrenal factor in the maintenance of essential hypertension is stressed in such early cases in which splanchnic section has not been successful.

REFERENCES

1. Keith, N. H., Wagener, H. P., and Barker, N. W.: Some Different Types of Essential Hypertension: Their Course and Prognosis, Am. J. M. Sc. **197:** 332, 1939.
2. De Takats, G., Heyer, H. H., and Keeton, R. W.: The Surgical Approach to Hypertension, J. A. M. A. **118:** 501, 1942.
3. Peet, M. M., and Isberg, E. M.: The Surgical Treatment of Arterial Hypertension, J. A. M. A. **130:** 467, 1946.
4. Smithwick, R. H.: Surgical Treatment of Hypertension; Some Suggestions About Selection of Cases for This Form of Therapy, J. M. Soc. New Jersey **44:** 304-316, 1947.
5. Hinton, W. J., and Lord, J.: Analysis of Surgical Failures and Fatalities Following Thoraco-Lumbar Sympathectomy for Essential Hypertension, New York State J. Med. **46:** 1715, 1946.
6. De Takats, G., Graupner, G. W., Fowler, E. F., and Jensik, R. J.: The Surgical Approach to Hypertension. Second Report, Arch. Surg. **53:** 111, 1946.
7. Page, J. H., Taylor, R. D., Corcoran, A. L., and Mueller, R.: Correlation of Clinical Types With Renal Function in Essential Hypertension. II. Effect of Spinal Anesthesia, J. A. M. A. **124:** 736, 1944.
   Gregory, R., and Levin, W. L.: Studies in Hypertension. V. Effect of High Spinal Anesthesia on the Blood Pressure of Patients With Hypertension and Far Advanced Renal Disease, J. Lab. & Clin. Med. **30:** 1037, 1945.

Gregory, R., Levin, W. L., Ross, G. T., and Bennett, A.: Studies on Hypertension, Arch. Int. Med. **77**: 385, 1946.

Southworth, M. L., and Russek, H. I.: A Technique for Testing Hypertensive Patients Preoperatively, Ann. Surg. **125**: 119, 1947.

8. De Takats, G., and Fowler, E. F.: The Surgical Treatment of Hypertension. III. The "Neurogenic" Versus Renal Hypertension From the Standpoint of Operability, SURGERY **21**: 773, 1947.
9. Trueta, J., Daniel, P., Barclay, A. E., Francis, K. J., and Pritchard, M. M. L.: Renal Pathology in the Light of Recent Neurovascular Studies, Lancet **2**: 237, 1946.

Barclay, A. E., Daniel, P., Franklin, K. J., Pritchard, M. M. L., and Trueta, J.: Records and Findings During Studies of the Renal Circulation in the Rabbit With Special Reference to Vascular Short-circuiting and Functional Cortical Ischemia, Proc. Physiol. Soc. in J. Physiol. **105**: 27, 1946.

10. Ogden, E., Collings, W. D., and Sapirstein, L. A.: A Change of Mechanism in the Course of Hypertension of Renal Origin. Experimental Hypertension, The New York Academy of Sciences **3**: 153, 1946.
11. Selye, H.: The General Adaptation Syndrome and the Diseases of Adaptation, J. Clin. Endocrinology **6**: 117, 1946.
12. Binger, C. A. L., Ackerman, N. W., Cohn, A. E., Schroeder, H. A., and Steele, J. M.: Personality in Arterial Hypertension, American Society for Research in Psychosomatic Problems, New York, 1945, Robert Brunner.
13. De Takats, G., and Cuthbert, F. P.: Effect of Suprarenal Denervation and Splanchnic Section on the Sugar Tolerance of Dogs, Arch. Surg. **30**: 151, 1935.
14. Sayers, G. M., Sayers, H., Fry, E. G., White, A., and Long, L. N. H.: The Effect of the Adrenotrophic Hormone of the Anterior Pituitary on the Cholesterol Content of the Adrenals, Yale J. Biol. & Med. **16**: 361, 1944.
15. Rinehart, J. F., Williams, O. O., and Capeller, W. S.: Adenomatous Hyperplasia of the Adrenal Cortex Associated With Essential Hypertension, Arch. Path. **32**: 169, 1941.

Perera, G. A.: The Relationship of the Adrenal Cortex to Hypertension. Observations on the Effect of Hypo-adrenalism on a Patient With Hypertensive Vascular Disease, J. A. M. A. **129**: 537, 1945.

16. Heinbecker, P.: Cushing's Syndrome, Medicine **25**: 225, 1944.
17. Adson, A. W., and Allen, E. V.: Essential Hypertension. The Treatment of Hypertension, Medical Versus Surgical, Ann. Int. Med. **14**: 233, 1940.
18. Craig, W. McK.: Personal communication.
19. Peet, M. M.: Personal communication.
20. Smithwick, R. H.: Personal communication.
21. Hinton, W. J.: Personal communication.
22. Grimson, K. S.: Personal communication.
23. Smithwick, R. M.: A Technique for Splanchnic Resection in Hypertension, SURGERY **7**: 1, 1940.
24. Poppen, J. L., and Lemmon, L.: The Surgical Treatment of Essential Hypertension, J. A. M. A. **134**: 1, 1947.
25. Grimson, K. S.: The Surgical Treatment of Hypertension. Collective Review, Surg., Gynec. & Obst. **75**: 421, 1942.
26. De Takats, G., and Helfrich, L. S.: Sterility of the Male After Sympathectomies, J. A. M. A. **117**: 20, 1941.
27. De Takats, G., and Walter, L. E.: The Control of Intractable Pancreatic Pain by Splanchnic Nerve Section. Surg., Gynec. & Obst. **85**: 742, 1947.
28. Weeks, G., Ryan, B. V., and Van Hoy, J. M.: Two Deaths Associated With Supradiaphragmatic Vagotomy, J. A. M. A. **132**: 988, 1946.
29. Blegen, H. M., and Kintner, A. R.: Aggravation of a Gastric Ulcer Following Dorsolumbar Sympathectomy, J. A. M. A. **133**: 1207, 1947.

PORTACAVAL ANASTOMOSIS

ARTHUR H. BLAKEMORE, M.D., NEW YORK, N. Y.

(From the Department of Surgery, Presbyterian Hospital)

THE operation of establishing an anastomotic junction between the portal and caval systems (portacaval shunt) for the relief of portal hypertension has now been accomplished by us in thirty-six cases. There have been five postoperative deaths. Aside from the development of technique, the experience has profited us most in the selection of cases for operation, the preparation of patients for operation, and their postoperative care.

Analysis of the five postoperative deaths and their contributions to our knowledge would seem worth while. One death from hemorrhage at the conclusion of the operation served, early in our experience, to emphasize the necessity for careful hemostasis. In this case a small vein in the great omentum had been torn and gone unobserved for a considerable period during the latter part of the operation.

Mesenteric thrombosis was the cause of death on the sixteenth postoperative day in a case of Banti's syndrome with a splenorenal anastomosis. This case was indeed a serious challenge to us of the advisability of continuing with the portacaval shunt procedure. A critical analysis of the case, however, revealed several points of interest: First, the anastomosis had been performed with meticulous care as to good blood vessel technique, asepsis, etc. It had been noted at the time, however, that the splenic vein was very large, thin walled, and saculated in areas whereas in other areas there were sclerotic plaques and in some places reduplication of the intima. Upon opening the anastomosis, blood was seen to flow from the splenic vein to the renal vein. The patient was allowed to be ambulatory early postoperatively and on about the sixth postoperative day distention of the abdomen with gas became progressively worse. This was followed by the appearance of ascites and increasing pain. Finally, by the fourteenth postoperative day the patient had a high temperature and during the next two days became moribund. We have noted in some other cases of Banti's syndrome degenerative changes in the splenic vein but not nearly so extensive as in this case. Largely on account of this fact we have instituted anticoagulant therapy postoperatively in cases where we can attain a reasonably dry operative field. With the organization of an anticoagulant team in the Presbyterian Hospital we have been able to carry out this therapy without serious mishap.

The case of mesenteric thrombosis served to point up two other factors in the postoperative handling of cases of portacaval anastomosis, namely: (1) control of postoperative distention, and (2) avoidance of early mobilization. It is our belief that a change in position from lying to upright before the soft tissues about an anastomosis have become stabilized by healing may well result in a slight shift of the soft parts, sufficiently to angulate or occlude by compression the anastomosed veins. Furthermore we are convinced that severe distention of the abdomen may accomplish the same undesirable result.

Presented at the annual meeting of the Society for Vascular Surgery, Atlantic City, N. J., June 9, 1947.

We find that severe postoperative distention can be avoided in the average case by the administration of Prostigmine and the use of a rectal tube at four-hour intervals. If the stomach is distended at operation we do not hesitate to pass a well-lubricated nasogastric tube and leave it in place connected with suction for a day or two postoperatively.

A third postoperative death was caused by cardiac failure. This was a case of Banti's syndrome in a 67-year-old woman who also suffered from hypertensive cardiovascular disease. The patient died on the fourth postoperative day. In retrospect we wonder if the patient would have benefited from early digitalization.

Our first major error in clinical judgment in the selection of cases for operation arose in a case of posthepatitis cirrhosis. A brief summary of this case serves to emphasize important factors governing the selection of cases for operation in this important group.

CASE REPORT

A 39-year-old man, in late February, 1945, developed epigastric discomfort, anorexia, and diarrhea with the passage of clay-colored stools. Coincident with these symptoms he developed pain and swelling of the legs.

The patient was admitted to the Presbyterian Hospital, March 7, 1945. On examination he was found to be slightly jaundiced. Two small tender nodules were noted, one in each thigh. Biopsy of one of the nodules proved it to be due to sporotrichosis. Further laboratory studies revealed a serum bilirubin of 4.5 mg. per cent, serum phosphatase 9.1, Bodansky units, cephalin flocculation test 3+, serum albumin 2.4 per cent; serum globulin 5.4 per cent; euglobulin 2.5 per cent; Kline 4+, Wassermann—alcoholic negative, cholesterin 3+. The prothrombin time was 75 per cent of normal. The patient had an afebrile course in the hospital but the jaundice and anorexia persisted. One month after admission the legs were swollen, ascites was present, but the liver and spleen could not be palpated. Laboratory findings were as follows: cephalin flocculation 3+, erythrocyte sedimentation rate 9.2, hemoglobin 13 Gm., red blood cells 4,810,000, white blood cells 4,550, platelets 140,000, prothrombin time 73 per cent of normal, serum bilirubin 3.5 mg. per cent, serum protein 7.8 per cent, albumin 2.2 per cent, globulin 5.6 per cent. May 8, 1945, esophograms were negative for esophageal varices. May 15, 1945, following a short period of periumbilical distress, the patient passed four bloody stools, the hematocrit fell to 29, hemoglobin, 8.5 Gm., and red blood cells 2,650,000. This first bleeding episode occurred exactly three months after onset of the patient's illness. Fourteen days after onset of hemorrhage a repeat esophogram revealed the presence of esophageal varices. The serum albumin fell to 1.9 per cent and the prothrombin time to 50 per cent of normal. Bromsulfalein retention thirty minutes after injection was 50 per cent. Intravenous hippuric acid liver function test revealed 0/6 Gm. excreted at the end of one hour. The patient's course after a 2½ months' stay in the hospital was, from every point of view, progressively downhill and this in spite of everything a medical regime had to offer. The occurrence of gastrointestinal bleeding plus the subsequent demonstration by x-ray examination of the presence of esophageal varices was proof of the presence of portal hypertension secondary to periportal fibrosis in the liver.

In view of these findings we were asked to consider the question of establishing a portacaval shunt. It was our first experience with this type of case and proved to be a bitter one. On June 7, 1945, approximately three months after onset of the hepatitis, we operated upon the patient, performing an end-to-side anastomosis of the portal vein to the vena cava. The patient very promptly developed cholemia and was dead on the third postoperative day.

The most informative necropsy findings were in the liver. This organ presented the picture of a healing subacute yellow atrophy (hepatitis) in which areas of nodular cirrhosis were interspersed with the areas of liver cell degeneration. There was no evidence of systemic sporotrichosis.

Whereas, from the clinical course prior to operation, it seems very improbable that this man would have recovered, on the other hand, it was an error to have operated upon him when we did. The persistently elevated cephalic flocculation test should have warned us of the presence of active hepatitis. The progressive fall in serum albumin to an extremely low level, the rise of the prothrombin time to high levels, and the marked retention of bromsulfalein were additional warnings of serious liver decompensation. The wiser course to have pursued in this case would have been to have replaced the blood losses from hemorrhage by transfusions with the hope that he would recover sufficient liver compensation to withstand a portacaval shunt procedure at some subsequent date. This case came along early in our experience, subsequently we have operated successfully upon a fair number of patients with posthepatitis cirrhosis. Unfortunately, it would seem that cirrhosis with portal hypertension is not an uncommon sequela to hepatitis.

I shall cite a recent case to illustrate that posthepatitis cirrhosis cases present the same threat of sudden death from hemorrhage as do cases of portal cirrhosis of the avitaminosis (alcoholic) type.

CASE REPORT

A girl 18 years of age in 1941 had infectious hepatitis, slight jaundice, with exacerbations. Four years later (November, 1945) the patient had the first episode of gastrointestinal bleeding. This was followed by ascites. In January, 1946, the patient was admitted to the Rockefeller Hospital for special study and treatment. She improved gradually with total disappearance of the ascites. In the fall of 1946 she had returned to college when suddenly, in October, she suffered from a severe hematemesis. In spite of intravenous glucose, transfusions, and intravenous liver extract, she lapsed into coma. Gradually after three days the coma began to clear. The ascites which had supervened was relieved by one paracentesis followed by several intravenous injections of serum albumin. The patient then did well until December, 1946, when she had the third episode of gastrointestinal bleeding. Following recovery from this, a liver biopsy was done. The liver was found to be markedly contracted and studded with large and small nodules. The small areas of regenerated liver cells were unevenly distributed with interposing masses of fibrous tissue. On Jan. 9, 1947, the patient had another spell of gastrointestinal bleeding at which time the hematocrit fell to 23. In spite of five transfusions the patient lapsed into semicoma from which she gradually recovered. On March 8, 1947, the patient suddenly developed an unexplained fever. Temperature rose to 105° F. Following the fever, ascites supervened which was gradually cleared with intravenous albumin. Unfortunately, however, following the last dose of albumin the patient had the fifth attack of gastrointestinal hemorrhage requiring four transfusions. To summarize, this girl had four episodes of severe gastrointestinal bleeding over a five-month period. The spleen had been appreciated as unusually large throughout this period and as evidence of hypersplenism she maintained a leucopenia, low platelet count (18,000), and a secondary anemia. On the other hand the albumin globulin ratio was not reversed. The serum albumin ranging better than 3 per cent, the bromsulfalein retention was only 23 per cent after forty-five minutes. The disconcerting findings concerning the liver were a maintained +++ cephalin flocculation, the episode of coma, and the more recent (March) unexplained fever in the presence of jaundice. The prothrombin time was slightly elevated, a finding which, in view of the good serum albumin level, we did not interpret as necessarily indicating liver decompensation. We have recorded moderate elevations of the prothrombin time in cases of portal hypertension with "hypersplenism" before—even cases of extrahepatic portal block in which the liver chemistry was normal.

It was decided* that the only hope for the patient was to attempt a portacaval shunt with removal of the very large spleen. Accordingly she was transferred to the Presbyterian Hospital. Operation was scheduled for May 1 and during induction with ether anesthesia the patient developed severe pulmonary edema necessitating postponement of the procedure. In view of the prompt recovery and the absence of cardiac pathology it was concluded that the anesthetic (ether) may have precipitated the attack of pulmonary edema.

During the ensuing twelve days the patient received two transfusions and two 25 Gm. doses of albumin intravenously. On May 13, 1947, under cyclopropane anesthesia the spleen was removed and the stump of the splenic vein was anastomosed end-to-side by suture, with the left renal vein. At operation the liver was found to be severely contracted and nodular. The spleen was five times normal size and the portal pressure measured 480 mm. of water. The patient's systemic blood pressure was well maintained throughout the operation and she left the operating table in good condition. Heparin was given intravenously at the instant of opening the anastomosis and anticoagulant therapy was maintained for nine days postoperatively. During postoperative convalescence the patient received 500 c.c. of blood, 500 c.c. of plasma, and 75 Gm. of albumin intravenously. There were no signs or evidence of acute liver failure during convalescence.

Our fifth postoperative death taught us much concerning the selection of cases of portal cirrhosis for operation. The case is described here.

CASE REPORT

A 58-year-old man previously had had eight admissions to the Presbyterian Hospital for plastic procedures to restore a nose which had partly been destroyed by a gumma. In November, 1945, the patient developed pain in the epigastrium coincident with which ascites appeared. He gave a long history of a moderate daily consumption of alcohol with not infrequent sprees. He had been treated for syphilis from 1925 to 1941. There was no history of jaundice. Appetite had never been good.

Examination of this patient on admission revealed a large abdomen (ascites) with wasting of the soft parts elsewhere. There was no jaundice but numerous spider angiomas were present. Following removal of 5,800 c.c. of ascitic fluid, a hard liver could be felt just at the costal margin. The spleen was not palpable.

The significant laboratory findings at the time were cephalin flocculation ++++; serum protein 5 per cent; albumin 2.7 per cent; globulin 2.3 per cent; prothrombin time 55 per cent of normal; bromsulfalein retention thirty minutes, 50 per cent. The presence of esophageal varices was demonstrable by x-ray examination.

After six weeks on a modern cirrhotic medical regime the patient's appetite began to improve. He gained ten pounds in weight. There was a very slight rise in blood proteins (albumin 3 per cent, globulin 2.8 per cent) but no appreciable lessening of the ascites. After four months' therapy there was no lessening of ascites. The cephalin flocculation test remained ++++; serum protein 5.8 per cent, albumin 2.9 per cent; globulin 2.9 per cent. After five months' therapy, serum protein was 5.3 per cent; albumin 2.6 per cent; globulin 2.7 per cent. The unrelenting drain on proteins resulting from the removal of 4 to 7000 c.c. of ascitic fluid every five to seven days was beginning to show on the total protein figure but worse to indicate the progressive decline in liver compensation—for the first time the blood albumin content had become lower than the globulin content.

After nine months' therapy the patient had no diminution in the ascites. Whereas the bromsulfalein retention was 10 per cent less than initially (40 per cent after thirty minutes), the blood proteins had consistently decreased (albumin 2.4 per cent, globulin 2.6 per cent). The galactose removal constant (intravenous) was 50 per cent of normal (2.2). Interestingly enough, however, the cephalin flocculation test, which was previously consistently ++++, had decreased to ++. The prothrombin time had not decreased materially over the nine-month period of observation.

On Sept. 26, 1946, approximately eleven months after the first symptoms of cirrhosis had appeared in this patient, a splenorenal anastomosis employing the nonsuture technique

*Dr. Allen Whipple very kindly joined me in consultation at the Rockefeller Hospital to help make a decision in this difficult case.

was performed. At operation the liver was found to be nodular and extremely atrophic. The spleen was fibrotic and approximately three times normal size. Measurement of the portal pressure revealed it to be in excess of 390 mm. of water.

The patient was given ether anesthesia. Early in the operation the blood pressure began to fall in spite of more than restitution of the blood loss. All in all the operation was accomplished with minimal blood loss and in record time, in spite of which the patient was in poor condition at the close of the operation.

The patient lived four days postoperatively, the last thirty-six hours of which he was in coma. The clinical picture was of a failing liver.

Reviewing the case in retrospect, there is no denying that the patient was doomed without operation. He had had thirty-nine paracentesis and for months had begged for surgical relief. Whereas he was entitled to an attempt at surgical relief the important question arises, what could we have done to increase the chances of his survival? We now know of several things we might have done to increase this man's chances of surviving a portacaval shunt procedure: (1) The use of cyclopropane anesthesia. We are now convinced that this is by far the best anesthetic for poor-risk patients with cirrhosis. (2) Preoperative and postoperative intravenous albumin therapy. We now have evidence that a blood albumin raised to a figure in excess of 3 per cent in a badly cirrhotic liver by the intravenous administration of albumin is likely to maintain this rise for a considerable period of time, that is, a period of time far in excess of that which can be accounted for on the basis of the amount of albumin in grams given. (3) The early use of Prostigmine at four-hour intervals postoperatively for the control of distention.

In conclusion we may summarize some of the most important information we have gleaned from our experience as follows: (1) The necessity for scrupulous hemostasis and the desirability of postoperative anticoagulant therapy. (2) The avoidance of operation in the presence of active hepatitis in cases of cirrhosis secondary to hepatitis. As our experience has shown, cirrhosis with evidence of portal hypertension may occur in some cases of infectious (virus) hepatitis before the latter is subsided. (3) The avoidance or postponement of operation in cases of cirrhosis, whatever the cause, when the liver is bordering on decompensation. It is not safe to rely too much on clinical signs unless they are confirmed by laboratory findings—jaundice, for example, of a slight degree may come and go in patients with cirrhosis but a deepening jaundice with an elevated cephalin flocculation would caution me to delay. Furthermore, it is true that some cirrhotic patients may have the most extreme depression of blood albumin, bromsulfalein, and other tests without a trace of jaundice. The sudden appearance of telangiectasia (spider angiomata) would justify a resurvey of the liver status before proceeding with operation.

In general, a patient with chronic cirrhosis who consistently shows an albumin between 2.5 and 3 per cent with a bromsulfalein retention in excess of 40 per cent thirty minutes after injection with or without an elevated prothrombin time is not a good risk for the portacaval shunt. Unfortunately, all too often such cases present themselves in which operation offers the only ray of hope. We now know that many of these patients can be eased through an operation successfully after a few weeks preparation with intravenous albumin, blood, and an intensive liver regime, followed by a careful postoperative handling.

CAUSALGIA

III. A General Discussion

Harris B. Shumacker, Jr., M.D., Indianapolis, Ind.

(From the Department of Surgery, Yale University School of Medicine, New Haven, Conn.)

THE painful condition following injury of peripheral nerves which we recognize as causalgia must have occurred from the earliest times. Its incidence in civilian life has undoubtedly been increased by the dangers associated with the more general and widespread use of industrial machinery, rapid means of transportation, and similar hazardous accompaniments of our modern civilization. It is a disorder, however, which has confronted the medical profession in particularly large numbers periodically as we have allowed ourselves to become embroiled in mass warfare. As each succeeding war tends to result in larger numbers of nonfatal battle casualties and as improved methods of treatment result in the conservation of more and more injured extremities, the problem of causalgia becomes of increasing military importance.

It is my purpose to discuss some general aspects of the problem of causalgia in the light of the early contributions and of recent studies. An attempt will be made to clarify the clinical picture and the treatment, and to make some comments concerning theories of the basic mechanism of pain. I shall also try to point out certain lines of investigation which I feel may contribute to our further understanding of this disorder.

I do not know who first observed and recorded this clinical syndrome. Certainly Denmark,[1] in 1813, described some features of the condition very accurately. Speaking of a soldier who had sustained a radial nerve injury from a musket-ball wound of the arm, he said:

> I found him labouring under excessive pain, which the largest opiate could not assuage. . . . The little sleep he had, if it could be called such, was disturbed by frightful dreams and starting. . . . He described the sensation of pain as beginning at the extremities of the thumb and all the fingers, except the little one, and extending up the arm to the part wounded. It was of a burning nature, he said, and so violent as to cause a continual perspiration from his face. He had an excoriation on the palm of the hand, from which exuded an ichorous discharge. The cause of this he ascribed to a shell rolling over it. His agonies, he observed, were insufferable, depriving him of sleep, and the enjoyment of his food, for which he had sometimes an appetite. He declared himself incapable of enduring it longer without some relief, and earnestly requested the removal of the arm.

The author further pointed out that touching or moving passively the affected hand caused exacerbation of the pain. After futile efforts to alleviate the pain with "warm and vapour baths, anodyne embrocations, etc.," an amputation was carried out with complete relief. Denmark had discussed with the patient "the possibility of saving the limb, and relieving the pain, by cutting down upon the nerve, and removing a part of it, above the wound."

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In 1838 Hamilton[2] described a peculiar redness of the skin, swelling, and contractures in certain cases of intense pain associated with partial paralysis of peripheral nerves. From the account of his patients it is evident that they were not examples of true causalgia as we now recognize this state.

Paget in 1864 described fully the glossy skin which may be associated with causalgia and pointed out its association with pain[3]:

> Glossy fingers appear to be a sign of peculiarly impaired nutrition and circulation due to injury of the nerves. They are not observed in all cases of injured nerves, and I cannot tell which are the peculiar conditions of the cases in which they are found; but they are a very notable sign, and are always associated, I think, with distressing and hardly manageable pain and disability. In well-marked cases, the fingers which are affected (for this appearance may be confined to one or two of them) are usually tapering, smooth, hairless, almost void of wrinkles, glossy, pink or ruddy, or blotched as if with permanent chilblains. They are also very painful, especially on motion, and pain often extends from them up the arm.

Though Paget recognized the association of glossy skin and a painful state, there is nothing in his discussion which would lead one to believe that he recognized or referred to the peculair condition which we know as causalgia.

In the same year appeared the monumental treatise on *Gunshot Wounds and Other Injuries of Nerves* by Mitchell, Moorehouse, and Keen[4] which contained their classic account of the disorder to which Mitchell subsequently applied the term "causalgia."[5] So vivid is their depiction of the condition that I feel justified in quoting them at some length.

> For these very reasons we have set apart for distinct consideration that kind of pain which we have before spoken of as burning pain. It is a form of suffering as yet undescribed, and so frequent and terrible as to demand from us the fullest description. . . . The terms here used may seem strong to those who have not encountered these cases; but no one who has seen them will think that, as regards some of them, it would be possible to overstate their most wretched condition.
>
> We have some doubt as to whether this form of pain ever originates at the moment of the wounding; but we have been so informed as regards two or three cases. . . . Certain it is that, as a rule, the burning arises later, but almost always during the healing of the wound.
>
> The seat of burning pain is very various; but it never attacks the trunk, rarely the arm or thigh, and not often the forearm or leg. Its favorite site is the foot or hand. In these parts it is to be found most often where the nutritive changes are met with; that is to say, in the palm of the hand, or palmar surface of the fingers, and in the dorsum of the foot; scarcely ever on the sole of the foot or the back of the hand. Where it first existed in the whole foot or hand, it always remained last in the parts referred to, as its favorite sites.
>
> The great mass of sufferers described this pain as superficial but others said it was also in the joints, and deep in the palm. If it lasted long, it was referred finally to the skin alone.
>
> Its intensity varies from the most trivial burning to a state of torture, which can hardly be credited, but which reacts on the whole economy, until the general health is seriously affected.
>
> The part itself is not alone subject to an intense burning sensation, but becomes exquisitely hyperaesthetic, so that a touch or a tap of the finger in-

creases the pain. Exposure to the air is avoided by the patient with a care which seems absurd, and most of the bad cases keep the hand constantly wet, finding relief in the moisture rather than in the coolness of the application. . . .

As the pain increases, the general sympathy becomes more marked. The temper changes and grows irritable, the face becomes anxious, and has a look of weariness and suffering. The sleep is restless, and the constitutional condition, reacting on the wounded limb, exasperates the hyperaesthetic state, so that the rattling of a newspaper, a breath of air, another's step across the ward, the vibrations caused by a military band, or the shock of the feet in walking, give rise to increase of pain. At last the patient grows hysterical, if we may use the only term which covers the facts. He walks carefully, carries the limb tenderly with the sound hand, is tremulous, nervous, and has all kinds of expedients for lessening his pain. In two cases, at least, the skin of the entire body became hyperaesthetic when dry, and the men found some ease from pouring water into their boots. They said, when questioned, that it made walking hurt less; but how or why, unless by diminished vibration, we cannot explain. One of these men went so far as to wet the sound hand when he was obliged to touch the other, and insisted that the observer should also wet his hand before touching him, complaining that dry touch always exasperated his pain.

Cold weather usually eased these pains; heat and the hanging down of the limb made them worse. Motion of the part was unendurable in some of the very worst cases; but, for the most part, it did no harm, unless so excessive as to flush the injured region.

The relations of burning pain to altered nutrition already received attention from us. It appears quite certain that in cases of glossy skin, burning always exists. It is also certain that it may exist without association with diseased skin; but that in these instances the evidence of depraved nutrient states will be very likely to follow upon the pain, should that symptom last very long.

The temperature of the burning part we have always found to be higher than that of surrounding parts, or than that of corresponding points on the other half of the body.

Mitchell and his associates elaborated further upon the glossy skin previously described by Paget. They found the skin deep red or red and pale in patches, the epithelium often partially denuded, leaving the cutis exposed in places, the subcuticular tissues generally shrunken, the integument tightly drawn and often cracked. They described the skin as "shining as though it had been skillfully varnished." In most patients the affected part was devoid of hair. In some a vesicular eczematous eruption was present, often recurring from time to time. The nails were curved with extreme lateral arching, with thickening of the skin underneath the end of the nail, and sometimes with retraction of the proximal end so as to leave sensitive matrix partly exposed. In their experience causalgia always occurred in cases of partial, and never in cases of complete, division of nerves. In the description of affected cases, darting, pricking, tingling, and other pains were described in addition to burning.

FURTHER COMMENTS ON THE SIGNS AND SYMPTOMS OF CAUSALGIA

From the foregoing it is apparent that causalgia as originally described was characterized by the following features: pain of varying intensity and predominantly burning in character, coming on some time after incomplete injury

to a peripheral nerve, felt chiefly in the periphery of the affected extremity, exacerbated by touching the part, dependency, jarring, emotional excitement, dryness, and generally by heat, relieved somewhat by wetness and cold, associated usually with glossy, red, blotched skin, always comparatively increased in warmth, and leading in many instances to emotional instability. In its essentials this has remained an accurate description of the condition. In certain details, however, further experience has revealed aberrations from this original account. For example, it has been evident for some time that the affected hand or foot is not invariably warmer, but sometimes colder, than the contralateral one.

Elsewhere my associates and I[6] have presented our experiences with regard to the signs and symptoms of causalgia. Much valuable information concerning the clinical features of this disorder has been presented in other reports of cases which were studied in the Armed Forces during World War II. It may be profitable to analyze these data.

As experience with causalgia has increased through the years it has become a generally accepted fact that this condition is particularly prone to occur following injury of the median or sciatic nerve. There was some involvement of the median nerve in 39 of our 49 cases of causalgia of the upper extremity, and of the sciatic nerve in 34 of 41 cases involving the lower extremity, while the tibial or peroneal divisions were affected in an additional 5 cases. It is of interest, however, that the ulnar nerve was injured in this series almost as frequently as was the median (37 cases as compared with 39). I have listed in Table I the available data on 230 recently reported cases.[6-10] In 80 of the 97 cases of causalgia of the lower extremity (82.5 per cent) the sciatic nerve was injured while the tibial and peroneal nerves were damaged alone or in combination in 11 of the remaining cases. In the upper extremity the median nerve was affected more frequently than any other nerve though the brachial plexus and various

TABLE I. NERVE LESIONS IN CAUSALGIA

	AUTHOR AND NUMBER OF CASES REPORTED					
NERVES INJURED	MAYFIELD & DEVINE	GOODMAN ET AL.	ULNER & MAYFIELD	KIRKLIN ET AL.	SHUMACKER ET AL.	TOTAL CASES
Brachial plexus	1		12	3	14	30
Median, ulnar, & radial			3		11	14
Median	7	7	9	28	7	58
Median & ulnar	1	3	7		7	18
Median & radial			1		1	2
Radial				1	4	5
Ulnar		1			4	5
Radial & ulnar					1	1
Sciatic	6		23	17	33	79
Sciatic & saphenous					1	1
Saphenous				3	2	5
Peroneal		1			2	3
Tibial		1	2		3	6
Tibial & peroneal			2			2
Femoral			1			1
Total	15	13	60	52	90	230

combinations of its three chief nerves were involved even more often. In the recent war, causalgia occurred more commonly in the upper extremity than in the lower. In a total of nearly 400 cases (Table II) the upper extremity was affected in 238, or 60 per cent.[6-12]

TABLE II. INCIDENCE OF CAUSALGIA IN UPPER AND LOWER EXTREMITIES

AUTHOR	EXTREMITIES INVOLVED, NUMBER OF CASES		TOTAL CASES
	UPPER	LOWER	
Mayfield & Devine	9	6	15
Ulmer & Mayfield	32	28	60
Rasmussen & Freedman	82	18	100
Allbritten & Maltby	23	44	67
Goodman et al.	11	2	13
Kirklin et al.	32	20	52
Shumacker et al.	49	41	90
Total	238 (60%)	159 (40%)	397

All of the cases described by Mitchell and his associates were examples of partial paralysis of nerves and certainly most of those subsequently reported have had incomplete nerve lesions. It has become evident, however, that causalgia may occur following complete paralysis. Pollock and Davis[13] observed that burning pain occurred once in their series of 38 cases in the presence of a complete lesion of the ulnar nerve. Leriche[14] and Freeman[15] have observed causalgia in the distribution of a nerve which had been completely divided, and Allbritten and Maltby[12] found the nerve completely divided in 2 of their patients. In our series of 90 cases the nerve injury was clinically complete in 11; these patients had neuromas in continuity, to be sure, and in none was the nerve found at operation to be divided with separation of the cut ends. Of perhaps similar significance is the fact that division and resuture of nerves is often ineffectual in bringing about relief of pain.

All of the recent observations emphasize the hazard of final evaluation of the status of peripheral nerve function from examinations carried out before relief of pain. Such examinations notoriously yield unreliable information, the apparent extent of nerve damage generally appearing much greater than is evident when the examination is repeated after pain has been eliminated. This observation is of some importance in reference to the question whether one's initial attack in causalgia should be directed toward relief of pain or to surgical attack upon the seemingly injured nerves.

Mitchell, Moorehouse, and Keen's skepticism concerning the occurrence of causalgic pain immediately after wounding is not borne out by recent studies. It is true that the patient's memory for details during and immediately after such a trying experience may be inaccurate. Nevertheless, approximately 50 per cent of patients with causalgia stated that the onset of pain was immediate. This was true in 36 of 98 patients reported by Rasmussen and Freedman, 44 of 75 reported by Ulmer and Mayfield, and in 50 of our 90 patients. Most of the other patients noted beginning of pain within the first week after injury.

In all of the patients studied by Mitchell, Moorehouse, and Keen the pain was described as burning in character though other types of pain were also

often present. It was the constancy of burning pain which led Mitchell to designate the clinical syndrome causalgia. Though burning is the usual and characteristic type of pain, otherwise indistinguishable cases in which the patient does not describe the pain as burning are occasionally seen. This absence of burning was found in about 10 per cent of the patients studied by Kirklin, Chenoweth, and Murphy and in 4.4 per cent of our patients. The only report with which I am familiar which includes a large number of cases of causalgia without burning pain is that of Rasmussen and Freedman; 45 of their 100 patients did not have burning. It is of interest that, although these authors stated that the clinical picture in these 45 patients was otherwise nearly identical with that in the remainder, they also said that the cases of minor causalgia reported by Homans were similar to their own. Most authors have not encountered cases of major causalgia without burning pain. Burning is certainly the common and predominant pain, but a small percentage of patients are seen who have no burning and are in every other respect suffering from typical causalgia. I do not feel that the absence of burning in such cases precludes a diagnosis of causalgia though etymologically the term is not strictly applicable to them.

In the original account it was pointed out that some relief of pain generally resulted from wet applications and often from exposure to cool weather. Such alleviation from moisture and cold has been encountered subsequently in a variable percentage of cases. Ulmer and Mayfield found that 68 of 75 patients experienced some relief and only 7 noted no effect from moisture. Almost one-half of the patients of Kirklin, Chenoweth, and Murphy obtained some amelioration of pain from local use of a wet cloth. Forty-four of the 100 patients studied by Rasmussen and Freedman had tried cold wet applications on their own initiative; 35 noted partial relief and 9 no effect. In our own series, alleviation of pain from moisture was experienced by only 17 of 90 patients. It has been the common finding that those patients with vasodilatation are apt to prefer cold and those with vasoconstriction warmth.[9] Vasodilatation of the injured extremity was present in most of the patients of Rasmussen and Freedman and three-fourths of them had less pain on cool rainy days. Fifteen of our patients obtained some relief from cold wet applications or from cool weather; 12 had some increase in warmth of the affected hand or foot. Four of the 7 patients who had amelioration from warm moist poultices or from warm weather showed evidence of vasoconstriction. It must be concluded that wet applications are by no means always effective in providing partial relief. Though warmth often helps those patients with vasoconstriction, and cold those with vasodilatation, there are many exceptions. Indeed 64 of our 90 patients noted no amelioration of pain from any environmental alteration. Kirklin, Chenoweth, and Murphy have emphasized the well-supported observation that such alleviation of pain is not a constant nor diagnostic feature of causalgia.

Though relief of pain from changes in the environment does not appear to be a constant feature of causalgia, alleviation of pain during sympathetic anesthesia seems to be characteristic of the disorder. This is a point recently emphasized by Doupe, Cullen, and Chance.[16] I have encountered nothing in recent reports or in my own experience to bring into question the validity of this feature of causalgia.

Kirklin and his associates have called attention to the constancy of exacerbation of pain from certain stimuli in all cases of true causalgia. In their experience, moving or touching the affected part, sudden jarring, loud noises, and emotional excitement were common causes for marked, sudden increase in pain. Our experience is in entire agreement. Touching or tapping the hand or foot, moving it passively, or having the patient use it actively were the commonest stimuli causing such reactions. The exaggeration of pain from touching the body, noises, hunger, and emotional excitement occurred commonly in the severer cases of causalgia and less often in milder cases.

The pain of causalgia is apparently always constant except perhaps in those with the mildest cases and in those who are improving spontaneously or from treatment. It is always felt most intensively in the periphery of the extremity and commonly only in the peripheral sensory distribution of the affected nerve, or predominantly in this area. Numerous examples are seen, however, in which the pain is also present outside the area innervated by the damaged nerve. Sometimes it tends to spread up the arm or forearm. As Mitchell and his associates originally pointed out, it is particularly likely to be localized on the palmar surfaces of the hands and fingers. In contrast to their observation, however, we found it was often felt predominantly in the sole of the foot.

Their belief that glossy skin was especially common in causalgia and that such "nutritive" changes in the skin never occurred in the absence of burning pain has not been supported by other studies. Pollock and Davis,[13] for example, encountered 41 cases of glossy skin unassociated with causalgia, and found glossy skin in only 8 of 38 cases of burning pain. Meige and Benisty[17] had felt that alterations in the muscles and in the articular and tendinous structures were the result of associated vascular lesions. Pollock and Davis, however, noted vascular lesions rarely in their cases. It has been my experience that glossy, tight skin, as well as abnormal curving of the nails, periarticular fibrosis, contractures, and marked atrophy of muscles and subcutaneous fat are particularly common in combined neurological and vascular lesions. Mayfield and Devine and Ulmer and Mayfield pointed out an association of the state of the skin and hair with the vasomotor status. According to them, the skin of those in vasodilatation was usually reddish, dry, and scaly, and the hair long and coarse, while in those with vasoconstriction the skin was usually thin, glistening, wet, the digits tapered, and the hair diminished. Such observations were noted in some of our patients though we did not find this association as commonly as they. In our patients, absence of sweating was found to occur particularly in those with relatively complete sensory loss, though this was not invariably the case.

Mitchell, Moorehouse, and Keen stated that the causalgic limb was always warmer than the contralateral one. For some time, however, it has been clear that some causalgic extremities present evidence of vasoconstriction. A survey of the literature reveals a rather amazing discrepancy concerning the occurrence of vasodilatation and vasoconstriction. Among the more recent reports, for example, we note that Wan[18] found vasodilatation and hyperhidrosis in his 20 patients, while Goodman, Messinger, and White encountered evidence of sympathetic overactivity with aggravation of symptoms in a cold environment in their 13 cases. Three of Mayfield and Devine's patients had coldness of the hand or

foot with thin, glistening skin and excessive sweating, while in 9 there was elevation of skin temperature with little or no sweating and increased growth of hair. The further report of this series by Ulmer and Mayfield did not give precise data concerning the vasomotor status. They stated, however, that those patients with vasodilatation generally obtained relief from cold, moisture, and vice versa, and that 38 patients preferred cold water, 30 warm water, and 7 noted no effect from moisture. Rasmussen and Freedman found that their early cases showed evidence of vasodilatation which sometimes persisted as long as six months, but that generally after several months moderate vasoconstriction ensued. This tendency for vasodilatation of the affected limb in early cases and vasoconstriction in cases of long standing has been mentioned by some observers in connection with other posttraumatic disorders of the Sudeck atrophy type. In the experience of others, however, who have recently reported on large series of cases of causalgia, no change in vasomotor status has been observed during rather long periods of observation.[6, 7, 9] My associates and I have made an effort to evaluate carefully the vascular status of our patients and though these studies were not as comprehensive as we should have desired them to be, I feel that they permitted us to detect at least gross aberrations from the normal. We were rather surprised to find that about one-third of our patients presented evidence of relatively normal vascular tonus. Most of the others had relative vasodilatation though some had distinct vasocontriction. The vasoconstriction was rarely intense and the vasodilatation not often complete. Indeed, I have not found any significant difference in the vascular responses of causalgic limbs and of extremities with peripheral nerve injuries without causalgia. From the data available it appears that the affected hand or foot is likely to have increased warmth in causalgia, just as in the noncausalgic extremity with injury of peripheral nerves, that in some cases vasoconstriction will be present, and that in a fairly significant percentage the vasomotor tonus will be relatively normal.

The essential diagnostic criteria of causalgia appear to be the presence of constant, spontaneous pain following partial or, more rarely, complete injury of peripheral nerves, generally, but not always, predominantly burning in nature, exacerbated by certain stimuli, and capable of temporary, complete, or nearly complete alleviation during sympathetic procaine anesthesia. These cardinal points, together with the other features which I have discussed, make the diagnosis of causalgia relatively simple, and permit its easy differentiation from such related disorders as phantom limb and amputation stump pain, minor causalgia, Sudeck's atrophy, and similar posttraumatic vasomotor states. Confusion exists only in the case of the few patients who have atypical causalgia-like states in whom one or more of the essential diagnostic findings are absent. These cases are difficult to fit into any one of the recognized clinical entities. It would appear wise for the present to designate them as cases of atypical causalgia.

TREATMENT

It is not my purpose to review here all the measures which have been tried in an effort to bring about relief in causalgia. Beginning with the local blister-

ing which Mitchell and his associates first employed, almost every conceivable type of medication, physiotherapeutic aid, and surgical operation has been given a trial. Most of these measures have been followed by unreliable, inconstant results, or have proved entirely inefficacious. Some of them are needlessly destructive, such as the complete division and resuture of an only partially injured nerve, extensive posterior root section, and cordotomy. I shall discuss particularly the role of sympathetic interruption in treatment, and especially the use of repeated procaine blocks and operations upon the ganglionated chain. Though successes have been reported with periarterial sympathectomy, this method has proved less reliable than the more direct attack upon the sympathetic chain.

I feel no hesitation in re-emphasizing the worth of sympathetic interruption. Doubt still exists concerning the usefulness of procaine blocks, and though patients successfully treated by sympathectomy have been reported in the literature from time to time for nearly twenty years, this method of treatment has in general not found its way into the common source books of learning. A survey of 5 of the most recent textbooks of neurology,[19-23] for example, reveals that such methods are mentioned in only one. The comments concerning treatment are most discouraging. One states, "For persistently painful neuritis, and for causalgia, surgical intervention has justified itself. The procedures in vogue embrace neurolysis, resection and immediate suture, intraneural injections of alcohol, and periarterial sympathectomy. With each and all of these, favorable results have been secured." Another advises, "Section of the nerve and suture may be required for permanent relief although the condition often passes away spontaneously in several months. Repeated infiltration of the peripheral fibers with novocaine may give permanent relief. When all other methods fail, rhizotomy or even cordotomy must be employed." In another text we find the following, "The treatment is extremely difficult. Most of the patients become addicted to opiates, as no other analgesics give relief. Many complain that the contact with the vessel in which the limb is immersed in warm water for relief causes more trouble than the relief is worth. When the pain is finally gone (in one or two years) or as soon as possible, massage should be instituted. When causalgia is due to a neuroma, resection at a higher level may give relief. Injections of acetyl choline have been recommended, but in my experience they have not produced results. Cobra venom is usually of no avail. When the pain finally does cease the addiction must be treated as a separate condition." Still another states, "The satisfactory treatment of causalgia is always difficult. The most effective method of relieving the pain is to excise the damaged portion of nerve and resuture it. This means, however, substituting for an incomplete lesion a complete one, with prolonged and possibly permanent disability. On the other hand, if medical treatment is unsuccessful and operation is to be undertaken months after the injury, excision of the damaged portion of nerve may be of no benefit and the pain may persist even after interruption of the spinothalamic tract in the cord. Generally it is wise to begin with medical measures and review the position after a month or two. . . . If . . . he is not making progress and especially if he is a neurotic individual, surgical treatment should be carried out. . . . If operative treatment is decided upon, either the damaged area

of the nerve must be excised and the nerve sutured, or the nerve must be injected with alcohol above the level of the lesion. . . . If local operation fails to give relief, section of the posterior roots or the opposite spino-thalamic tract in the spinal cord must be considered, but these measures will often prove ineffective.'' The only reference to sympathectomy is the following, contained in a discussion of median nerve causalgia, ''Of late dorsal sympathectomy has been advocated for causalgia.''

I have cited these recommendations in no criticism of the authors. Most of the extensive experience with sympathetic interruption in the treatment of causalgia has been only recently reported. So many methods of treatment, subsequently proved ineffective, had been originally reported as successful that these authors may have been justified in overlooking the early case reports of relief from sympathectomy. I have felt, however, that the recommendation of often ineffectual and sometimes harmful measures in texts widely consulted by students and practitioners emphasizes the need for better understanding and broader appreciation of more reliable methods of treatment.

I do not know for certain who first utilized sympathetic interruption in causalgia. In 1927, after speaking of the good results which he had obtained during the preceding ten years with periarterial sympathectomy and excision of thrombosed vessels, Leriche[24] said, ''In case of failure, or of very diffuse pain, section of the rami communicantes would be indicated. I have never had occasion to do this. But I have operated in this fashion, as I am going to mention, in painful syndromes very like causalgia, and cure has been obtained. I believe that one will thus avoid having to resort to more mutilating rhizotomies and cordotomies.'' In 1929 Petit-Dutailles, Blamoutier, and Peron[25] reported a patient with apparently atypical causalgia whom they treated first by sectioning all the rami between the lower border of the superior cervical and the first thoracic ganglia. There was temporary relief after this procedure and after periarterial sympathectomy which they next carried out. Finally they excised the middle and divided the rami to the lower three-fourths of the superior cervical ganglion. Though the patient had residual hyperesthesia of the face and ear, the original pain was relieved. In 1930 appeared Spurling's[26] clear-cut report of complete relief of pain following excision of the second dorsal ganglion and division of the rami to the first dorsal and stellate ganglia. Other cases were reported from time to time; for example, Kwan's[27] case in which the stellate and second dorsal ganglia were excised. Cases such as this one emphasized the real value of sympathectomy, for the patient had previously undergone, without any relief, a neurolysis, a brachial periarterial sympathectomy, and then a further neurolysis with excision of an obliterated scarred axillary artery.

It is only within the past few years, however, that the results of large series of cases treated by sympathectomy are available for analysis. In Table III I have summarized data concerning 257 patients recently treated in this manner. I have attempted to divide the cases into those with excellent, good, and poor results. When the relief of pain has been described as complete, or when only trivial pain persisted, or when the author has listed the result of operation as affording ''relief'' without qualification, I have considered the result to be

excellent. When there was persistence of some pain but when the patient's course was so favorably altered that no further treatment was required, I have considered the outcome as good. Under "poor" are listed the few instances of trivial relief or of complete failure. Some of the failures undoubtedly occurred in examples of atypical and not true causalgia as was the case in the single failure in our own experience.[6, 28] It is evident that excellent results were obtained in 196 patients, or 76.3 per cent, good results in 54, or 21 per cent, and poor results in only 7, or 2.7 per cent. Excellent results are somewhat more frequent in causalgia of the upper (82.9 per cent) than in causalgia of the lower extremity (65.6 per cent). In our own experience it appeared clear that the results were better in cases of severe causalgia than in the milder cases. Most of the recent reports contain no statement concerning this point, but Rasmussen and Freedman noted no correlation between the severity of the pain and the degree of relief afforded by operation.

TABLE III. RESULTS OF SYMPATHECTOMY IN CAUSALGIA

AUTHOR	DORSAL SYMPATHECTOMY				LUMBAR SYMPATHECTOMY				ALL			
	NO.	EXC.	GOOD	POOR	NO.	EXC.	GOOD	POOR	NO.	EXC.	GOOD	POOR
Goodman et al.	11	9	2	0	2	1	1	0	13	10	3	0
Kirklin et al.	33	24	9	0	15	9	5	1	48	33	14	1
Rasmussen & Freedman	36	26	7	3	5	2	3	0	41	28	10	3
Mayfield & Devine	6	6	0	0	6	6	0	0	12	12	0	0
Ulmer & Mayfield	30	30	0	0	26	26	0	0	56	56	0	0
Allbritten & Maltby	8	5	2	1	22	6	15	1	30	11	17	2
Shumacker et al.	34	31	2	1	23	15	8	0	57	46	10	1
Total	158	131	22	5	99	65	32	2	257	196	54	7

Some interesting aspects of the problem have been raised by recent observations. According to Rasmussen and Freedman the results of treatment in causalgia of the upper extremity were better when a preganglionic rather than a postganglionic operation was carried out. Allbritten and Maltby and Ulmer and Mayfield have had experiences suggesting that it is desirable and sometimes necessary to sympathectomize the area of injury as well as the area to which the pain is referred. The former had a patient with a popliteal wound who was not relieved by third and fourth lumbar ganglionectomy but obtained complete relief after excision of the first and second ganglia. The latter had 3 patients with wounds of the buttocks who failed to improve after second, third, and fourth lumbar ganglionectomy but had no pain after excision of the first. Two others were not relieved by first, second, third, and fourth lumbar ganglionectomy but were subsequently cured by removal of the eleventh and twelfth dorsal ganglia. Kirklin, Chenoweth, and Murphy have questioned the interpretation of these results, feeling that it is fanciful to suppose that a few failures are dependent upon inadequate extent of sympathectomy when the majority of patients with wounds of the thighs and buttocks are cured without excision of

the first lumbar or the lower thoracic ganglia. I do not think that the two sets of observations are incompatible. We know well enough that when the first ganglion is included in a lumbar ganglionectomy the skin of the entire thigh and leg is sympathectomized according to sweating and skin resistance tests, and that only the leg and posterior surface of the thigh are denervated when the first ganglion is left intact.[29, 30] As yet we do not know the extent of sympathetic denervation of the deeper structures following excision of various segments of the lumbar and lower thoracic chain. Since the site of the disturbed neural mechanism which presumably initiates the pain may vary even though the skin injury is in the same location, it may be that one case is properly denervated by a less extensive operation and another only by a more complete ganglionectomy. Furthermore, there is still some question whether cure in causalgia is not effected by interruption of afferent pain fibers in the peripheral sympathetics. If such afferent fibers are present, their precise pathway is not mapped out, and although the distribution of the sympathetic efferents has been found to vary little and to follow a fairly regular pattern, any existing afferents may have a much more variable course.

I would feel that the available data suggest that at least a small number of the incomplete cures or failures following sympathectomy are explainable upon the basis of inadequate sympathetic denervation. Obviously any such cases encountered in the future should be subjected to higher sympathetic procaine blocks in order to see whether the residual pain can be relieved. Certain of the failures have occurred in cases which are almost certainly examples of atypical causalgia-like states rather than true instances of causalgia. Undoubtedly one explanation of some residual pain after operation concerns the persistence of paresthesias and mild pain of the sort commonly found in cases of peripheral nerve injury without causalgia. It is easy to understand that a patient with pain of various types should feel more acutely any remaining discomfort once the more severe and predominant pain is relieved. I have commonly observed, indeed, in cases of causalgia and in cases of peripheral neuritis undergoing subsidence of symptoms, an apparent elevation to conscious appreciation of certain paresthesias which were not complained of beforehand when a more intense pain was present. Such mechanisms undoubtedly account for certain cases of residual discomfort after sympathectomy. It is perhaps significant that these residual symptoms tend to diminish with the passage of time and often to disappear rather quickly in contrast to the course of events in most untreated cases of causalgia. It is also almost certainly true that residual pain is perpetuated in a few instances by neuropsychiatric factors. Everyone is in agreement with the original opinion of Mitchell that long-persistent severe causalgia tends to disrupt the patient's emotional balance. Cases have been observed in which it appears that persistent complaints were dependent upon psychiatric factors and in which these symptoms have subsided with reassurance. Lidz and Payne[31] have reported one case of causalgia, perhaps atypical in certain aspects, in which psychiatric measures were the sole treatment responsible for relief of symptoms. There is not, however, any evidence that the pain of causalgia is primarily initiated by any psychiatric mechanism.

There is general agreement concerning the efficacy of sympathectomy in the treatment of causalgia. There is, however, considerable disagreement concerning the usefulness of procaine blocks as a therapeutic measure. Ulmer and Mayfield state that none of their patients obtained complete and permanent relief from blocks alone. Allbritten and Maltby had two patients who were permanently relieved by a single procaine block but in their experience repeated blocks usually did not produce permanent relief. Kirklin, Chenoweth, and Murphy stated that infrequently a series of blocks relieved the pain to such an extent that no operative interference was necessary but that usually no lasting effect was noted. On the other hand, Rasmussen and Freedman obtained satisfactory results with blocks alone in 45 of 91 patients treated. In 13 of these patients the results obtained were excellent and in 32 the result was good; in none of them was further treatment required. My associates and I obtained excellent results in 21 cases from one or more procaine blocks. I am thoroughly convinced that certain individuals can be treated satisfactorily by blocks alone. Our experience with sympathetic anesthesia therapy in causalgia is similar to that which I, and others, have had with other conditions sometimes amenable to sympathetic blocks. If the initial block gives relief for an interval of time prolonged beyond the period of sympathetic anesthesia or if repeated blocks result in relief for successively longer periods of time, one should be encouraged to continue such treatment. If the initial block, on the other hand, gives relief limited to the period of sympathetic anesthesia or, more particularly, if successive blocks give relief for the same or diminishing periods, one should abandon these measures and proceed with operation.

There is every evidence that the good results from sympathetic blocks and sympathectomy are the result of transient or permanent interruption of sympathetic innervation and not of some nonspecific suggestive mechanism. I have never seen pain disappear during the course of a sympathetic injection before the needle tip was introduced into the neighborhood of the sympathetic chain; relief of pain occurred only after this area was infiltrated with procaine. Pain was not relieved in the case of the few injections which were ineffectual in producing sympathetic anesthesia. Ulmer and Mayfield had 2 patients in whom they did not obtain the desired denervation of the upper extremity because of inadvertent removal of the fourth rib instead of the third and decentralization of the third and fourth instead of the second and third ganglia; in these patients pain was not relieved. Kirklin, Chenoweth, and Murphy described some of their patients as having had incomplete denervation of the extremity according to skin resistance tests, and stated that they noted no difference in the therapeutic result in the patients completely and incompletely denervated. These observations are somewhat puzzling to me. I have studied many patients by skin resistance and sweating tests after dorsal or lumbar sympathectomy carried out essentially as they performed them, and have always found the denervation complete according to the recognized pattern for the particular operation performed.[29, 30] The only exceptions have been during the transient phase of apparent sympathetic activity which is not uncommonly noted from about the fourth to the eighth postoperative day.

The question naturally arises whether one's initial effort should be directed toward any required operation upon the injured nerves or toward the problem of relief of pain. It is true that the chance of adequate restoration of nerve function is better if neurolysis or neurorrhaphy is carried out early, and under no circumstances should such needed surgery be delayed any more than is necessary. According to Freeman, proper débridement, neurolysis, and neurorrhaphy in early cases are much more likely to bring about relief of pain than in cases of longer standing. I have not had experience with the early treatment of causalgia. It may be advisable to do appropriate surgery first upon the injured nerves in early cases of causalgia. It may also be proper in the mild cases of causalgia of longer duration to attack the injured nerves first and to delay any other necessary treatment of pain until a later date. With regard to severe causalgia, with the possible exception of the patients seen very early, I am convinced that the initial effort should be directed to relief of pain by sympathetic block or sympathectomy.

This point of view is taken for several reasons. In the first place, sympathetic interruption generally achieves a prompt and gratifying result, while operations upon the injured nerves rarely bring about diminution of pain. The pain must be abolished as soon as possible in order to avoid the profound mental and emotional changes, as well as the general physical deterioration, which so frequently occur if pain continues unabated. From a simple humane point of view one cannot condone long-continued suffering. To attempt to give some respite from opiates only courts drug addiction with all its tragic sequelae. Furthermore, relief of pain must be obtained in order to prevent useless damage to the affected extremity. The patient with severe causalgia will not use the injured hand or foot; not even passive physiotherapy is tolerated. He runs, therefore, a great risk of undergoing extreme wasting of the muscles, and the development of periarticular fibrosis and disabling contractures. These risks of local damage which may prevent eventual recovery of serviceable function are far greater than are entailed in a delay of a few weeks in freeing or repairing the damaged nerves. Indeed, there is a real difficulty in performing proper nerve surgery as the initial procedure in causalgia because neurological tests may be so misleading in these patients. Almost invariably the nerve disfunction in the causalgic limb appears to be greater than is actually the case. Nerves only partially paralyzed may appear to be completely paralyzed, and uninjured nerves may appear to be damaged. It is striking how much better the nerve function is seen to be when examination is repeated after the pain has been abolished. Unfortunately, the true state of nerve damage is not always evident even during the transient period of freedom from pain which follows procaine infiltration of the sympathetic chain. If nerve surgery is to be attempted before pain is permanently relieved, however, neurological examination should at least be performed during a period of sympathetic procaine anesthesia.

The approach to the treatment of causalgia which I have outlined is based upon the fact that this disorder is likely to go on unremittingly for an indefinite period of time, contrary to the rather optimistic inference of Mitchell and others that the difficulty is self-limited and tends to subside spontaneously after a

period of months or at most a year or two. Numerous cases are recorded in which the pain has persisted for many years. Indeed when John Mitchell[32] reviewed his father's cases thirty years later he found that a considerable number of the patients had continued to have pain for many years after they had been originally treated. Very few instances of spontaneous subsidence of pain have been observed in recent series of cases even though some of the patients have been studied months or even a year or more after the injury.

THE MECHANISM OF PAIN

Numerous theories have been proposed to explain the fundamental basis of, and the nerve pathways involved in, the pain of causalgia and other allied painful states. Great credit is due to those who have proposed these theories for they have required careful observation and ingenious thinking. It is fair to say, however, that, in the light of our current knowledge, no theory yet offered furnishes an entirely satisfactory explanation of the pain of causalgia. I do not propose to discuss all the theories and I have no new concept to offer. I feel, however, that it may be worth while to discuss some aspects of the question. The problem centers about the relief of pain afforded by sympathetic interruption.

It would appear to be evident that certain theories which explain the relief of pain from sympathetic interruption as a consequence of alteration of blood flow are not applicable in all cases. Lewis[33] has felt that relief of pain is achieved by bringing about increased blood flow to the affected limb. Yet it is certainly true that many patients with causalgia present no evidence of vasoconstriction and that many obtain no relief whatsoever by the induction of extreme vasodilatation by means other than sympathetic interruption. De Takats[34] assumed that the pain is due to a state of chronic capillary dilatation, and that blocking of sympathetic impulses is effective by bringing about arteriolar dilatation and capillary constriction. I know of no extensive studies of capillary microscopy in causalgia. Typical causalgia may be present without gross evidence of capillary dilatation. To be sure, the capillaries may be atonic and dilated in the presence of general vascular constriction, as in Raynaud's disorder. Yet in those cases of Raynaud's disease with the most marked capillary atony and dilatation which I have observed, causalgic pain is not present. Finally, as I have mentioned previously, arteriolar dilatation induced by indirect body heating or direct warming of the limb is generally ineffectual in relieving pain. Further observations which may be interpreted as mitigating against alteration of blood flow as the correct explanation of the relief afforded by sympathetic interruption in causalgia and allied painful states concern the problem of phantom limb pain. In this condition pain is present in the absence of the distal part of the extremity—the part primarily subject to changes in vascular tonus. It has been a common observation that reamputation at a higher level generally fails to give relief, and it is also quite evident that in some of these cases pain ceases with blocking of sympathetic impulses.[35]

Currently the two most widely accepted theories are those of Livingston[35] and Doupe, Cullen, and Chance.[16] Livingston's explanation involves an irritative focus resulting from the trauma, afferent impulses arising from this trigger

point and setting up an abnormal state of activity in the "internuncial pool" in the spinal cord, and resultant initiation of abnormal motor responses from both lateral and anterior horn neurons. Relief from sympathetic interruption or from any other method of treatment is felt to result because of a breaking of the vicious circle. This clever theory invokes certain concepts which are without objective proof. Though it is ostensibly a satisfactory explanation, I feel that it leaves something to be desired. One wonders why interrupting the cycle by sympathetic block or sympathectomy is almost invariably successful and interrupting it by nerve section, careful débridement, or lysis of nerves is so often unsuccessful. It is difficult to explain why the cycle cannot be broken more readily by other methods which presumably alter the state of sympathetic activity, such as the production of reflex vasodilatation with apparent quiescence of sympathetic function. The question also arises as to why the effects of the internuncial pool action upon the efferents should vary so remarkably regarding the state of sympathetic activity.

Doupe, Cullen, and Chance explained the pain of causalgic states upon an alteration in excitability of adjacent sensory fibers by the sympathetic impulses continually at play as a result of emotional stress, the process of thermoregulation, and from various other stimuli. Though there is much to commend this theory, I feel that it is challenged somewhat by the constant relief afforded by sympathetic block and the frequent lack of effect upon pain of alteration of sympathetic activity by other means. No one can deny that some efferent sympathetic impulses may be discharged rather continuously. Yet it has been generally assumed, for example, that a relative, if not complete, inhibition of sympathetic efferent impulses occurs in reflex vasodilatation. From what is known of sympathetic action one would certainly be forced to assume that sympathetic efferent activity must vary enormously with the marked changes in vascular tonus which we recognize as representing states of extreme vasoconstriction and extreme vasodilatation. According to their theory it is understandable that pain might rarely be completely relieved by any method of altering vascular tonus other than by sympathetic anesthesia or operative sympathectomy, but one would assume that such maneuvers should rather regularly alter the severity of the pain. Consequently, the validity of the theory is brought into question by the failure of such methods to influence the pain at all in many cases. Doupe, Cullen, and Chance, Rasmussen and Freedman, Harvey,[36] and I have studied cases of causalgia and of other allied painful states in which extreme vasoconstriction induced by such measures as local cooling, general body cooling, subcutaneously or even intra-arterially administered adrenalin have not altered the pain. Extreme vasodilatation induced by such measures as local heat, reflex vasodilatation, reactive hyperemia, and Prostigmine given intra-arterially have failed to affect the pain in any appreciable way. Yet sympathetic block has brought about prompt and complete relief in these same cases.

Obviously, assumption of the existence of afferent pathways in the peripheral sympathetics would enable one to explain the pain of causalgia and its relief by sympathetic interruption in a most satisfactory manner. The variable

status of efferent sympathetic activity in these cases would offer no challenge; in case of neuritis of somatic nerves we have numerous examples of relatively normal, hyperactive or hypoactive motor function. There have been a number of authors who have chosen to invoke the presence of afferent pain fibers in the peripheral sympathetics in reference to the pain of causalgia and related states (Foerster,[37] Shaw,[38] Middleton and Bruce,[39] Leriche[14]). Unfortunately no positive proof has been advanced by them.

The chief objection raised has been the lack of anatomic proof of such pathways. It is no more fanciful, however, to postulate their existence than to postulate without anatomic confirmation the presence of a new "nocifensor" set of nerves as Lewis[40] did in explaining certain painful states. Indeed, there are some data suggesting that such afferent nerves are demonstrable. Kuntz and Farnsworth,[41] for example, felt that they had histological evidence of such fibers and concluded, "Any operation which effectively eliminates the vasomotor innervation of an extremity must also divide a goodly number of afferent fibers supplying the blood vessels and other sympathetically innervated tissues in the area affected." Treadgill[42] cited the earlier work of Dogiel as having demonstrated both motor and sensory nerve cells in the stellate ganglia of dogs.

The experiments of Burget and Livingston[43] and of Moore and Singleton[44] have been extensively quoted as demonstrating physiologically the absence of afferent sympathetic pain fibers. In these experiments a painful reaction is elicited by intra-arterial injection of an irritating solution whether or not the extremity is sympathectomized; no pain reaction follows the injection when somatic anesthesia has been produced. These experiments are clear-cut and are easily confirmed. The pain reaction does not occur, however, if the solution is held within a segment of the main artery, but only if it is allowed to reach the terminal branches. The question naturally arises whether it constitutes a true stimulus for eliciting "sympathetic pain" or is merely another somatic pain stimulus having its effect once the irritant has diffused outside the vascular bed.

It is of interest that Treadgill[42] has recently reported experiments which suggest, on the other hand, that there are afferent pathways in the peripheral sympathetics. They depend upon the presence of a reaction to intense burning in an anesthetic limb with intact sympathetic innervation not present when the sympathetic chain has been excised, and upon the presence of a blood pressure response to intra-arterial injection of sodium lactate in a limb denervated by anterior and posterior root section but not elicited when the sympathetic chain has also been removed. Unfortunately experiments upon only 4 animals are reported, and further substantiation of this work is desirable before it can be accepted as proof of the existence of afferent fibers in the sympathetics.

Certain clinical observations, even though they do not offer conclusive proof, are highly suggestive of the existence of afferent pain fibers in the sympathetic nerves. For example, Freeman[45] observed a number of paraplegic patients with pain in whom a cordotomy producing analgesia up to a level two segments higher than the site of injury failed to relieve the constant dull aching

or burning pain, though the intermittent types of pain had ceased; these same patients were completely free of pain after a cordotomy performed at the second dorsal level. Operations which gave levels of analgesia at any point below the fourth thoracic dermatome often failed to relieve burning pain but all pain was relieved if the level was at or above the third dorsal dermatome. Since this type of pain was not affected by operations which severed the central pathways of the somatic pain fibers from the entire area in which the pain was felt and from the area of injury but was cured by a higher cordotomy, he felt that the most plausible explanation lay in the transmission of the pain impulses through fibers in the sympathetic nerves entering the cord at a high level. I have already referred to other suggestive clinical observations. Still other personal observations I present apologetically since they are inadequately controlled, but I do so in the hope that they may stimulate similar, but better controlled, observations. I have treated several patients with severe causalgia in whom complete relief of pain occurred promptly after procaine infiltration in the region of the sympathetic chain some time before thermocouple readings revealed any rise in skin temperature. This occurrence reminds one of the sensory anesthesia which so often precedes motor paralysis in spinal anesthesia or somatic nerve block. One cannot assume, however, that efferent sympathetic paralysis occurred after subsidence of pain at the time the increase in skin temperature was first noted; vasodilatation may have preceded the rise in skin temperature and may have occurred simultaneously with cessation of pain. Constant digital plethysmographic tracings as well as skin-temperature and skin-resistance measurements in such cases should settle the matter one way or the other. I have treated a few patients in whom the causalgic pain was not relieved by spinal anesthesia which was adequate for comfortable exposure of the lumbar sympathetic chain and for full vasodilatation of the lower extremities; in these same patients the pain ceased promptly with excision of the sympathetic chain. Such observations are highly suggestive of the existence of afferent pain fibers in the sympathetic nerves. Unfortunately, only a few such observations were made and in none of them was the precise level of anesthesia carefully checked, though the level must have been as high as the seventh dorsal segment since there was no pain in the operative incision.

It may be concluded that none of the current theories of the mechanism of pain is entirely satisfactory and that further intensive study is required.

SUMMARY

I have reviewed the early and recent contributions to the problem of causalgia and have attempted to discuss the signs and symptoms, the vasomotor status, the treatment, and the mechanism of pain. Much of the broad experience with this disorder was obtained only recently as a consequence of World War II. Though every effort was made to segregate such cases in special centers where the best opportunity existed for their careful evaluation and treatment, it is nevertheless true that the enormous volume of work, the limited personnel, and the lack of availability of certain apparatus precluded particular studies

which in retrospect would have been informative. It is unlikely that an opportunity will again present itself for study of such large groups of cases. It is entirely possible, however, that intensive study of fewer cases may settle some of the remaining problems.

It would seem important to study the vasomotor responses in each patient by every available method, including digital plethysmography and venous occlusion plethysmographic blood flow methods whenever possible. It will be profitable to pursue further the reaction of patients to alterations in the state of vascular tonus induced by various methods, and to study the effect of a variety of drugs affecting autonomic function, including such agents as tetraethylammonium chloride. It will be important to correlate better the time of onset of vasodilatation and of pain relief following sympathetic block, and to evaluate carefully any persistence of pain during spinal anesthesia. Particular study must be made of cases of incomplete relief of pain after sympathectomy. The so-called atypical causalgias require further clarification. Finally, it is hoped that more animal experimentation may throw new light upon the problem of the nerve pathways and the mechanism of pain. Better understanding of the fudamental problems connected with major causalgia may be of aid in understanding more clearly the other allied painful states.

REFERENCES

1. Denmark, A.: An Example of Symptoms Resembling Tic Douloureux, Produced by a Wound in the Radial Nerve, Med. Chir. Trans. **4**: 48-52, 1813.
2. Hamilton, J.: On Some Effects Resulting From Wounds of Nerves, Dublin J. M. Sc. **13**: 38-55, 1838.
3. Paget, J.: Clinical Lecture on Some Cases of Local Paralysis, Med. Times & Hosp. Gaz. **1**: 331-332, 1864.
4. Mitchell, S. W., Moorehouse, G. R., and Keen, W. W.: Gunshot Wounds and Other Injuries of Nerves, Philadelphia, 1864, J. B. Lippincott Company.
5. Mitchell, S. W.: Injuries of Nerves and Their Consequences, Philadelphia, 1874, J. B. Lippincott Company.
6. Shumacker, H. B., Jr., Speigel, I. J., and Upjohn, R. N.: Causalgia II, The Signs and Symptoms, With Particular Reference to Vasomotor Disturbances, To be published.
7. Mayfield, F. H., and Devine, J. W.: Causalgia, Surg., Gynec. & Obst. **80**: 631-635, 1945.
8. Goodman, E. N., Messinger, W. J., and White, J. C.: Indications and Results of Surgery of the Autonomic Nervous System in Naval Personnel, Ann. Surg. **124**: 204-217, 1946.
9. Ulmer, J. L., and Mayfield, F. H.: Causalgia. A Study of 75 Cases, Surg., Gynec. & Obst. **83**: 789-796, 1946.
10. Kirklin, J. W., Chenoweth, A. I., and Murphy, F.: Causalgia. A Review of Its Characteristics, Diagnosis, and Treatment, SURGERY **21**: 321-342, 1947.
11. Rasmussen, T. B., and Freedman, H.: Treatment of Causalgia; an Analysis of 100 Cases, J. Neurosurg. **3**: 165-173, 1946.
12. Allbritten, F. R., Jr., and Maltby, G. L.: Causalgia Secondary to Injury of the Major Peripheral Nerves, SURGERY **19**: 407-414, 1946.
13. Pollock, L. J., and Davis, L.: Peripheral Nerve Injuries, New York, 1933, Paul B. Hoeber, Inc.
14. Leriche, R.: The Surgery of Pain, Baltimore, 1939, Williams & Wilkins Company.
15. Freeman, N. E.: Cited by Allbritten and Maltby.[12]
16. Doupe, J., Cullen, C. H., and Chance, G. Q.: Post-traumatic Pain and the Causalgia Syndrome, J. Neurol., Neurosurg. & Psychiat. **7**: 33-48, 1944.
17. Meige, H., and Benisty, A.: Lesions vasculaires associees aux blessures des nerfs, Rev. neurol. **30**: 631, 1916.
18. Wan, F. E.: Sympathetic Causalgia. Report of Twenty Cases Treated by Sympathectomy, Chinese M. J. **61**: 1-13, 1943.
19. Brain, W. R.: Diseases of the Nervous System, ed. 2, London, 1940, Oxford University Press.

20. Wilson, S. A. K., and Bruce, A. N.: Neurology, Baltimore, 1940, Williams & Wilkins Company.
21. Nielsen, J. M.: A Textbook of Clinical Neurology, New York, 1941, Paul B. Hoeber, Inc.
22. Wechsler, J. S.: A Textbook of Clinical Neurology, ed. 5, Philadelphia, 1943, W. B. Saunders Company.
23. Grinker, R. R.: Neurology, ed. 3, Springfield and Baltimore, 1943, Charles C Thomas, Publisher.
24. Leriche, R.: Resultats de la chirurgie de la douleur, Presse méd. **1**: 561-564, 1927.
25. Petit-Dutailles, D., Blamoutier, and Peron, N.: Névrite avec causalgie du plexus brachial consécutive à une blessure de guerre. Amélioration après intervention sur le sympathique cervical, Rev. neurol. **1**: 1087-1091, 1929.
26. Spurling, R. G.: Causalgia of the Upper Extremity. Treatment by Dorsal Sympathetic Ganglionectomy, Arch. Neurol. & Psychiat. **23**: 784-788, 1930.
27. Kwan, S. T.: The Treatment of Causalgia by Thoracic Sympathetic Ganglionectomy, Ann. Surg. **101**: 222-227, 1935.
28. Shumacker, H. B., Jr., Speigel, I. J., and Upjohn, R. H.: Causalgia. I. Sympathetic Interruption in Treatment, Surg., Gynec. & Obst. **86**: 76-86, 1948.
29. Shumacker, H. B., Jr.: Sympathectomy in the Treatment of Peripheral Vascular Disease, SURGERY **13**: 1-26, 1943.
30. Richter, C. P., and Woodruff, B. G.: Changes Produced by Sympathectomy in the Electrical Resistance of the Skin, SURGERY **10**: 957-970, 1941.
31. Lidz, T., and Payne, R. L., Jr.: Causalgia. Report of Recovery Following Relief of Emotional Stress, Arch. Neurol. & Psychiat. **53**: 222-225, 1945.
32. Mitchell, J. K.: Remote Consequences of Injuries of Nerves and Their Treatment, Philadelphia, 1895, Lea Bros. & Co.
33. Lewis, T.: Pain, New York, 1942, The Macmillan Company.
34. De Takats, G.: Nature of Painful Vasodilatation in Causalgic States, Arch. Neurol. & Psychiat. **50**: 318-326, 1943.
35. Livingston, W. K.: Pain Mechanisms. A Physiologic Interpretation of Causalgia and Its Related States, New York, 1943, The Macmillan Company.
36. Harvey, A. M.: Personal Communication.
37. Foerster, O.: Der Leitungsbahen des Schmerzegefuhls und die Chirurgische Behandlung der Schmerzzustande, Berlin, 1927, Urban & Schwarzenberg.
38. Shaw, R. C.: Sympathetic System and Pain Phenomena, Arch. Surg. **27**: 1072-1080, 1933.
39. Middleton, D. S., and Bruce, J.: Post-traumatic Osteodystrophy at Joints, Tr. Med.-Chir. Soc. Edinburgh **113**: 49-72, 1933.
40. Lewis, T.: The Nocifensor System of Nerves and Its Reactions, Brit. M. J. **1**: 431-435, 1937.
41. Kuntz, A., and Farnsworth, D. I.: Distribution of Afferent Fibers via the Sympathetic Trunks and Gray Communicating Rami to the Brachial and Lumbosacral Plexuses, J. Comp. Neurol. **53**: 389-399, 1931.
42. Treadgill, F. D.: Afferent Conduction Via the Sympathetic Ganglia Innervating the Extremities, SURGERY **21**: 569-574, 1947.
43. Burget, G. E., and Livingston, W. K.: The Pathway for Visceral Afferent Impulses From Forelimb of the Dog, Am. J. Physiol. **97**: 249-253, 1931.
44. Moore, R. M., and Singleton, A. O.: Studies on the Pain Sensibility of Arteries. II. Peripheral Paths of Afferent Neurons From the Arteries of the Extremities and of the Abdominal Viscera, Am. J. Physiol. **104**: 267-275, 1933.
45. Freeman, L. W.: Personal communication.

EXPERIMENTAL CARDIAC HYPERTROPHY

The Acute Effect of Pulmonic and Aortic Stenosis

Frank Gerbode, M.D., and Arthur Selzer, M.D., San Francisco, Calif.

(From the Departments of Surgery and Medicine, Stanford University School of Medicine)

CARDIAC hypertrophy has been studied experimentally by the reproduction of various cardiovascular lesions which are known, in clinical medicine, to be associated with enlargement and hypertrophy of the heart. Aortic regurgitation may be produced by cutting an aortic cusp with a valvulotome passed through the carotid artery or left ventricle. As a result of this lesion, general cardiac hypertrophy developed, the most marked effect being in the left ventricle.[1, 2, 3] An experimental interventricular septal defect produced by piercing the septum with a knife valvulotome introduced through the left ventricle resulted in hypertrophy of both ventricles.[4] Similar results were obtained with arteriovenous fistulas,[5] and in this lesion hypertrophy was shown to be reversible by repair of the fistula.[6, 7] The left ventricle will hypertrophy in response to the stimulus of experimental hypertension, and experimental hyperthyroidism will cause hypertrophy of both ventricles.[8] Constriction of the pulmonary artery or the aorta led to hypertrophy of the ventricle affected by the experimental stenosis.[9, 10]

The most important factor producing hypertrophy of the heart is increased work, which is brought about in these experimental lesions either by increased pressure in the affected ventricle (hypertension, valvular stenosis), or by the effort necessary to propel an increased volume of blood (valvular insufficiency, septal defects, arteriovenous or arteriopulmonary connections). Though the broad relationship between increased cardiac work and hypertrophy is generally though not unanimously accepted, many questions in connection with this problem still remain unanswered.

Thus, the rate of hypertrophy of cardiac muscle has attracted little attention. Stewart[1] was able to recognize some hypertrophy one week after the production of an experimental lesion, while Herrmann,[2] using similar methods, concluded that weeks or months elapsed before definite hypertrophy developed.

The purpose of this study was to investigate the rapidity of hypertrophy of cardiac muscle in response to an adequate stimulus and to determine whether under these circumstances hypertrophy is a continuous process, extending over a long period of time. During the study a satisfactory method of producing acute pulmonic or aortic stenosis was developed. This and a few convincing results justify a report at this time.

TECHNIQUE

Stenosis of the proximal aorta or pulmonary artery can be produced by several methods. A broad cotton or silk ligature may be applied tightly

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enough to reduce the caliber of the vessel one-third to one-half. This is a relatively simple method, but frequently erosion of the vessel wall occurs, resulting in fatal hemorrhage. The same objection is found when metallic bands are used.[3, 10] To obviate this difficulty Holman[10] placed loose ligatures around the aorta and pulmonary artery in puppies. As the animals increased in size the

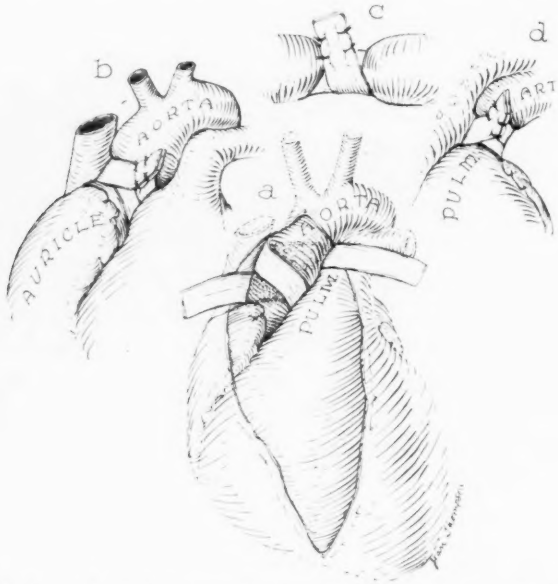

Fig. 1.—*a* and *b*, Technique of producing aortic stenosis with preserved fascia lata; *c*, side view; *d*, pulmonic stenosis.

vessel remained constricted at the site of the ligature, resulting in a gradually developing stenosis. This method, however, is not suitable for the study of the rate of growth of the cardiac muscle, where an acute stenosis of a high degree is desirable. We have found that a strip of preserved fascia lata, sutured around the great vessels in a figure-of-eight manner, will maintain the stenosis

TABLE I. AORTIC AND PULMONIC STENOSIS (THREE WEEKS' DURATION)

EXPERIMENT NO.	VESSEL STENOSED	BODY WEIGHT IN GRAMS AT NECROPSY	HEART WEIGHT IN GRAMS AT NECROPSY	PROPORTION HW TO BW	BOUGIE SIZE		MEAN THICKNESS OF VENTRICLE IN MM.
					AT STENOSIS	BEYOND STENOSIS	
5 female (9 mo. old)	Aorta	6900	70	.0101	15	28	10(Left)
Control female Litter mate		6200	46	.0074		28	7(Left)
17 male (3 mo. old)	Aorta	5400	38	.0070	32	38	8(Left)
Control female Litter mate		6100	33	.0054		38	6(Left)
15 male (3 mo. old)	Pulmonary artery	4150	43	.0104	15	24	6(Right)
Control male Litter mate		4300	27	.0063		24	4(Right)

adequately without erosion of the vessel wall (Fig. 1). A frequent complication resulting from an acute constriction of the aorta or pulmonary artery is heart failure resulting from the sudden increase in intraventricular pressure. This difficulty was partially overcome by the gradual production of the stenosis, in several stages, at ten-minute intervals. Animals then survived with a higher degree of stenosis, and the mortality from heart failure dropped considerably.

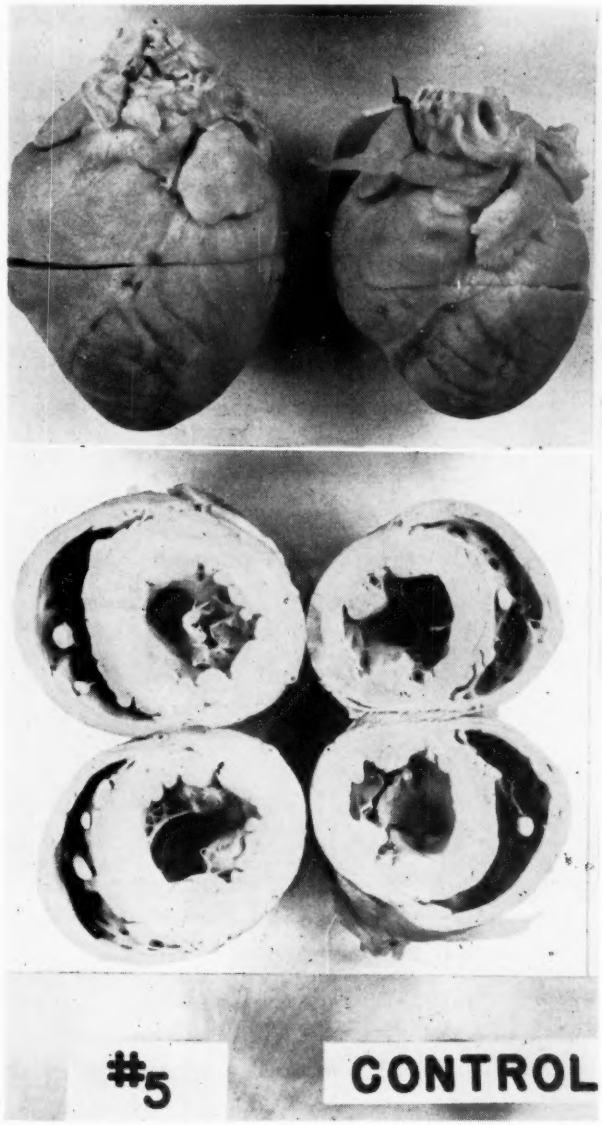

Fig. 2.—Aortic stenosis, three weeks. Note the gross enlargement of the heart as compared with the control. In the cross section view the left ventricles are placed side by side to show the increased thickness of the ventricle wall in the animal operated upon.

METHOD

The dogs were anesthetized with intravenous nembutal. Respirations were controlled with an intratracheal tube and a mechanical respirator. Using sterile

precautions, the heart was exposed by resecting the third or fourth rib, and the pericardium was opened. Either the proximal aorta or pulmonary artery was separated from its adjacent structures, and the fascial band was placed around the vessel. After gradually tightening it for about forty minutes, several sutures were placed to hold the degree of stenosis created. The pericardium was approximated loosely with a few interrupted sutures, the lung was inflated, and the chest was closed in layers. The animals were sacrificed after varying time

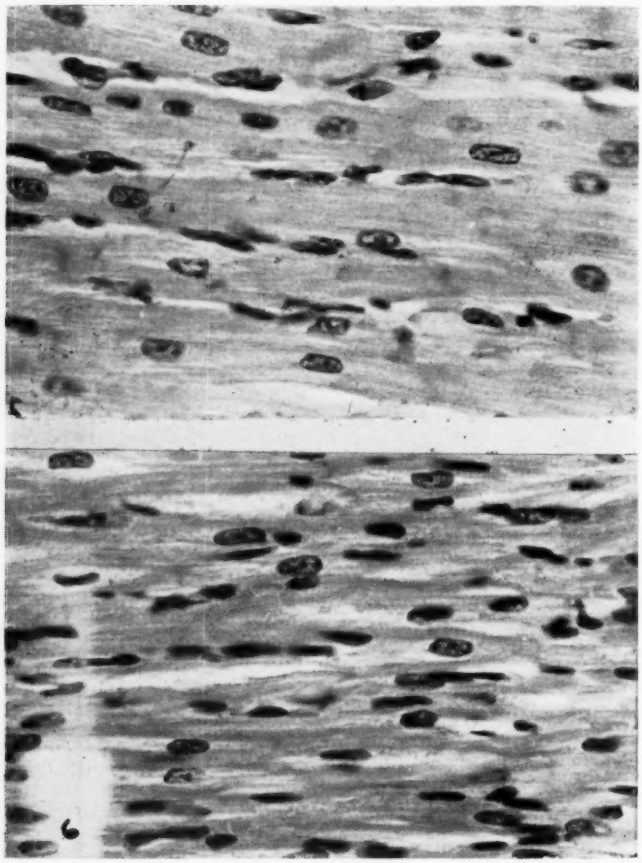

Fig. 3.—Microphotographs of the left ventricle in Experiment 5 (upper), an aortic stenosis of three weeks' duration, as compared with its control (lower). Note the marked increase in the cytoplasm of the muscle fibers causing separation of the nuclei.

intervals. The body weight at necropsy was recorded, the heart removed, and the degree of stenosis and the caliber of the vessel just beyond the stenosis were measured with bougies. After trimming away the pericardium, excess fat, and great vessels, the hearts were washed free of blood, emptied, and weighed. They were then fixed in formalin for one week, and thereafter cut transversely at similar levels, so that the thickness of the wall could be measured. Microscopic slides were made from like areas in the experimental and control animals.

RESULTS

In the first seven experiments adult dogs were used, being sacrificed after a period of one to four weeks. Aortic stenosis was produced in six of these ani-

mals, and pulmonary stenosis in one. It was thought that the heart weight to body weight ratio, as determined by Herrmann,[11] could be used as a standard control for these experiments. His studies of 200 dog hearts revealed a mean heart weight-body weight ratio of .00798, with a minimum of .00600 and a maximum of .00994. Using Herrmann's methods for determining the heart weight-body weight ratio, we found the following values in the first seven

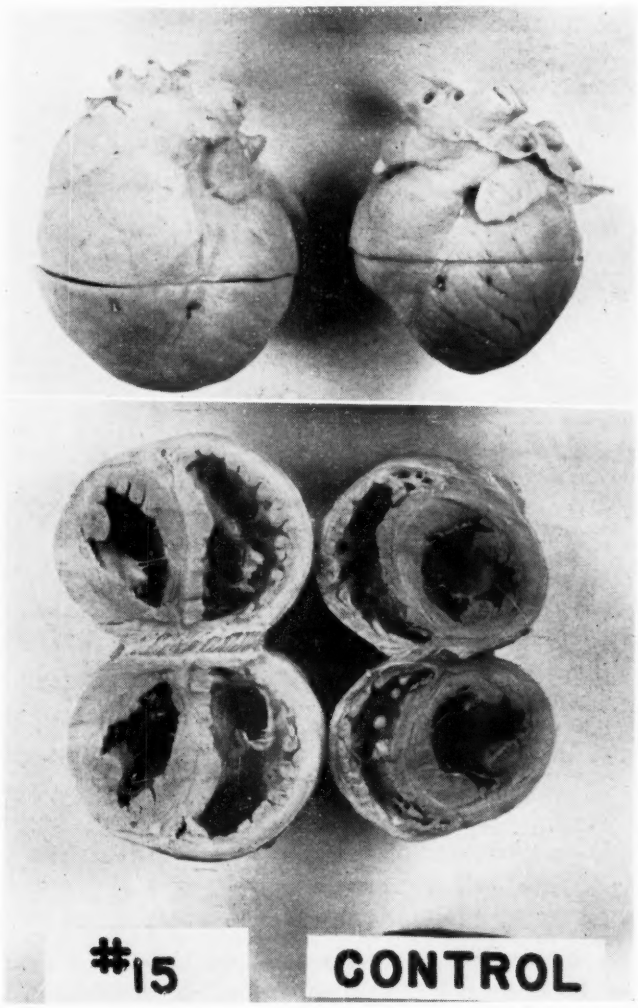

Fig. 4.—Pulmonic stenosis, three weeks. The right ventricle is markedly enlarged, as compared with the control. The cross section view is shown with the right ventricles in apposition to illustrate the increase in thickness of the ventricular wall in the animal operated upon.

experiments: .0078, .0080, .0085, .0090, .0101, and .0115. Although six of the seven ratios were above Herrmann's mean, only the last two could be accepted as indicating definite hypertrophy. These two instances occurred in an animal with pulmonary stenosis of three weeks' duration and in an aortic stenosis of four weeks' duration. For the most part these experiments merely indicated that acute hypertrophy was occurring in response to the stimulus of stenosis.

It was realized that a more accurate measure of the degree of hypertrophy could be obtained if carefully matched litter mates were used, retaining one animal as a control.

Seven experiments were performed on litter mates, all of them young animals. In six of these aortic stenosis was created, and in one pulmonary stenosis. Two sets of animals were sacrificed after one week, one after two weeks, and four after three weeks. In four experiments no definite hypertrophy was

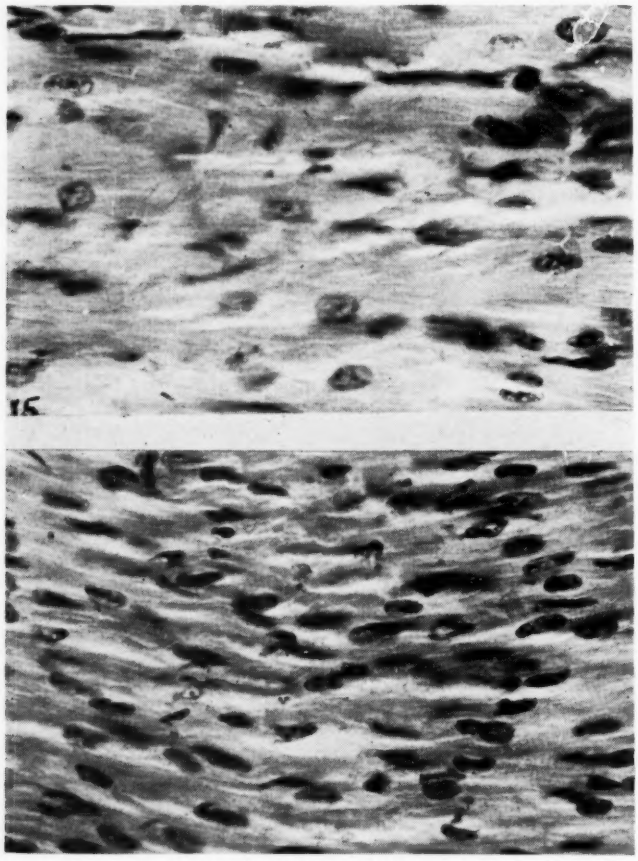

Fig. 5.—Microphotograph of a section of the right ventricle in Experiment 15 (upper), a pulmonic stenosis of three weeks' duration, compared with its control (lower). Note the enlarged muscle fibers in the animal operated upon.

found, and in all of these the stenosis was found to be very slight. Three experiments, all of them in the three-week group, were successful, and showed marked cardiac hypertrophy. The results are presented in Table I. Fig. 2 shows the gross specimen of Experiment 5 (aortic stenosis), with the litter mate control; Fig. 3 shows the microscopic section of the left ventricle, clearly indicating hypertrophy of the muscle fibers, as compared with the control animal. Figs. 4 and 5 present the gross findings and a microphotograph of a section of the right ventricle in the case of pulmonary stenosis, and the control.

DISCUSSION

In our experimental study of cardiac hypertrophy there were two variables: the degree of stenosis, acting as a stimulus for cardiac hypertrophy, and

the time factor. It was felt that the only reliable criterion of cardiac hypertrophy is the increase in muscle mass, and other evidence such as roentgenographic appearance, measurements of the heart and thickness of the heart wall, though recorded, were considered as only secondary. In order to simplify the problem the general heart weight was determined, rather than separate weights of cardiac chambers, for even the best methods of division of the heart may introduce a new error.

While the relationship between the increase in cardiac weight and the degree and duration of the stenosis will be the subject of a detailed study, one fact has been established: It was shown that with an adequate stimulus, definite hypertrophy develops within three weeks. The degree of hypertrophy, which in Experiment 15 amounted to a 65 per cent increase over the control animal, is comparable to the results of Holman, Herrmann, and others whose experiments extended over a period of many months. This would indicate that hypertrophy of the heart can be an acute process with most of the growth occurring within a short time after the stimulus for hypertrophy is established.

SUMMARY

A method of producing experimental aortic and pulmonary stenosis is described which enabled us to establish a high degree of stenosis with a low mortality. It was shown that pulmonic or aortic stenosis causes definite hypertrophy of the right or left ventricle within three weeks, the degree of which is comparable with the hypertrophy found in experimental stenosis of many months' duration.

REFERENCES

1. Stewart, Hugh A.: An Experimental Contribution to the Study of Cardiac Hypertrophy, J. Exper. Med. **13**: 187-209, 1911.
2. Herrmann, George R.: Experimental Heart Disease: II. The Effect of Experimental Aortic Regurgitation on the Heart Weight; With a Consideration of Some Factors Concerned in Cardiac Hypertrophy and a Summary of the Manifestations of Experimental Heart Disease, Am. Heart J. **1**: 485-507, 1925.
3. Eyster, J. A. E., Meek, Walter J., and Hodges, F. J.: Cardiac Changes Subsequent to Experimental Aortic Lesions, Arch. Int. Med. **39**: 536-549, 1927.
4. Holman, Emile, and Beck, Claude S.: The Physiological Response of the Circulatory System to Experimental Alterations. I. The Effect of Intracardiac Fistulae, J. Exper. Med. **42**: 661-679, 1925.
5. Holman, Emile: Arteriovenous Aneurysm. Abnormal Communications Between the Arterial and Venous Circulations, New York, 1937, The Macmillan Company.
6. Drury, Alan N., and Wightman, K. J. R.: Observations Relating to Cardiac Hypertrophy in the Rabbit: Its Production by Arterio-venous Anastomosis, Quart. J. Exper. Physiol. **30**: 45-57, 1940.
7. Drury, Alan N.: Observations Relating to Cardiac Hypertrophy Produced in the Rabbit by Arterio-venous Anastomosis: Effect of Closure of Anastomosis, Quart. J. Exper. Physiol. **33**: 107-112, 1945.
8. Rytand, David A., and Dock, W.: Experimental Concentric and Eccentric Cardiac Hypertrophy in Rats, Arch. Int. Med. **56**: 511-520, 1935.
9. Holman, Emile, and Beck, Claude S.: The Physiological Response of the Circulatory System to Experimental Alterations. III. The Effect of Aortic and Pulmonic Stenosis, J. Clin. Investigation **3**: 283-298, 1926.
10. Holman, Emile: Hemicardiac Hypertrophy Due to Increased Peripheral Resistance; A Study of Pulmonic and Aortic Stenosis Experimentally Produced, J. Thoracic Surg. **9**: 262-273, 1940.
11. Herrmann, George R.: Experimental Heart Disease; I. Methods of Dividing Hearts; With Sectional and Proportional Weights and Ratios for Two Hundred Normal Dogs' Hearts, Am. Heart J. **1**: 213-231, 1925.

THE RELATIONSHIP BETWEEN GROSS TYPE OF GASTRIC CARCINOMA AND ANACIDITY

ROBERT HEBBEL, M.D., AND DAVID GAVISER, M.D., MINNEAPOLIS, MINN.

(From the Departments of Pathology and Surgery, University of Minnesota Medical School)

WHILE most patients with gastric carcinoma have achlorhydria at the time the diagnosis is established, a significant number have free acid in at least some degree. It seemed worth while to determine whether, in our material, the presence or absence of achlorhydria bears any constant relationship to the gross type of carcinoma and whether, among patients with free acid, there is any unusual deviation from normal ranges of acidity in relation to any type of carcinoma. With reference to these points the results of a review of 284 cases in which gastric resection was performed are presented.

MATERIAL

For this study we have selected, from among those cases in which gastric resection had been performed, all cases in which both gastric acidity had been determined and the resected specimen was available for re-examination. The data to follow concern 284 such cases.

The carcinomas were classified according to the method of Borrmann[1]: Type I, polypoid carcinoma; Type II, sharply demarcated, ulcerating carcinoma; Type III, partly sharply demarcated, partly infiltrating carcinoma; Type IV, diffusely infiltrating carcinoma. This classification is convenient to use but has no special advantages over others and, as with any classification, one must sometimes be arbitrary as to the designation of a given tumor. The classification makes no distinctions on the basis of size of a tumor. Thus a Type IV tumor might be apparently limited to a small area or might obviously infiltrate the whole stomach.

The acid determinations varied as to method. Although a fractional analysis after histamine stimulation had been employed for the great majority, alcohol had been used in some cases and, in a few, only fasting samples had been analyzed. In all cases the highest recorded value for free acid was noted and those cases where free acid was present were further subdivided according to whether the values exceeded or were less than 20 degrees. Those cases in which the record clearly showed that histamine had been employed as the test substance were also considered separately. This maneuver eliminated some cases in which there was free acid on fasting samples and also eliminated others in which though histamine had been undoubtedly employed, the fact was not clearly shown in the record. The results of consideration of this restricted group, 239 cases, are, however, comparable to those of the entire group.

PRESENTATION OF DATA

These data appear in the accompanying tables where acidities are considered with reference to age, sex, and gross type of carcinoma. Table I shows the dis-

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TABLE I. RELATION OF GROSS TYPE OF TUMOR TO ACID SECRETION AMONG 205 MALES

AGE (YR.)	TYPE I					TYPE II					TYPE III					TYPE IV					ALL CASES				
	NUMBER	ACHLORHYDRIA	FREE ACID LESS THAN 20°	FREE ACID MORE THAN 20°	TOTAL WITH FREE ACID	NUMBER	ACHLORHYDRIA	FREE ACID LESS THAN 20°	FREE ACID MORE THAN 20°	TOTAL WITH FREE ACID	NUMBER	ACHLORHYDRIA	FREE ACID LESS THAN 20°	FREE ACID MORE THAN 20°	TOTAL WITH FREE ACID	NUMBER	ACHLORHYDRIA	FREE ACID LESS THAN 20°	FREE ACID MORE THAN 20°	TOTAL WITH FREE ACID	NUMBER	ACHLORHYDRIA	FREE ACID LESS THAN 20°	FREE ACID MORE THAN 20°	TOTAL WITH FREE ACID
28-40	0					1	1				2	1		1	1	2	2				5	4	0	1	1
41-50	1	1				3	2		1	1	5	2	1	2	3	13	7	3	3	6	22	12	4	6	10
51-60	1	1				12	10	1	1	2	9	7	1	1	2	25	15	4	6	10	47	33	6	8	14
61-70	1	1				30	23	3	4	7	16	12	1	3	4	41	22	4	15	19	88	58	8	22	30
71-83	2	2				9	7	0	2	2	11	8	1	2	3	21	13	3	5	8	43	30	4	9	13
Total	5	5				55	43	4	8	12	43	30	4	9	13	102	59	14	29	43	205	137	22	46	68

TABLE II. RELATION OF GROSS TYPE OF TUMOR TO ACID SECRETION AMONG 79 FEMALES

AGE (YR.)	TYPE I					TYPE II					TYPE III					TYPE IV					ALL CASES				
	NUMBER	ACHLORHYDRIA	FREE ACID LESS THAN 20°	FREE ACID MORE THAN 20°	TOTAL WITH FREE ACID	NUMBER	ACHLORHYDRIA	FREE ACID LESS THAN 20°	FREE ACID MORE THAN 20°	TOTAL WITH FREE ACID	NUMBER	ACHLORHYDRIA	FREE ACID LESS THAN 20°	FREE ACID MORE THAN 20°	TOTAL WITH FREE ACID	NUMBER	ACHLORHYDRIA	FREE ACID LESS THAN 20°	FREE ACID MORE THAN 20°	TOTAL WITH FREE ACID	NUMBER	ACHLORHYDRIA	FREE ACID LESS THAN 20°	FREE ACID MORE THAN 20°	TOTAL WITH FREE ACID
28-40	0					0					1	0	0	1	1	4	2	1	1	2	5	2	1	2	3
41-50	0					1	1				0					5	2	1	2	3	6	3	1	2	3
51-60	2	2				7	6	1	0	1	1	0	1	0	1	12	6	2	4	6	22	14	4	4	8
61-70	0					11	7	2	2	4	2	1		1	1	13	9	1	3	4	26	17	3	6	9
71-81	2	2				5	0	2	3	5	0					13	10	2	1	3	20	12	4	4	8
Total	4	4				24	14	5	5	10	4	1	1	2	3	47	29	7	11	18	79	48	13	18	31

TABLE III. RELATION OF GROSS TYPE OF TUMOR TO ACID SECRETION IN 284 CASES

AGE (YR.)	TYPE I					TYPE II					TYPE III					TYPE IV					ALL CASES				
	NUMBER	ACHLORHYDRIA	FREE ACID LESS THAN 20°	FREE ACID MORE THAN 20°	TOTAL WITH FREE ACID	NUMBER	ACHLORHYDRIA	FREE ACID LESS THAN 20°	FREE ACID MORE THAN 20°	TOTAL WITH FREE ACID	NUMBER	ACHLORHYDRIA	FREE ACID LESS THAN 20°	FREE ACID MORE THAN 20°	TOTAL WITH FREE ACID	NUMBER	ACHLORHYDRIA	FREE ACID LESS THAN 20°	FREE ACID MORE THAN 20°	TOTAL WITH FREE ACID	NUMBER	ACHLORHYDRIA	FREE ACID LESS THAN 20°	FREE ACID MORE THAN 20°	TOTAL WITH FREE ACID
28-40	0					1	1				3	1	0	2	2	6	4	1	1	2	10	6	1	3	4
41-50	1	1				4	3	0	1	1	5	2	1	2	3	18	9	4	5	9	28	15	5	8	13
51-60	3	3				19	16	2	1	3	10	7	2	1	3	37	21	6	10	16	69	47	10	12	22
61-70	1	1				41	30	5	6	11	18	13	1	4	5	54	31	5	18	23	114	75	11	28	39
71-83	4	4				14	7	2	5	7	11	8	1	2	3	34	23	5	6	11	63	42	8	13	21
Total	9	9				79	57	9	13	22	47	31	5	11	16	149	88	21	40	61	284	185	35	64	99

TABLE IV. RELATION OF GROSS TYPE OF TUMOR TO ACID SECRETION IN 239 CASES WITH KNOWN HISTAMINE STIMULATION

AGE (YR.)	TYPE I					TYPE II					TYPE III					TYPE IV					ALL CASES				
	NUMBER	ACHLORHYDRIA	FREE ACID LESS THAN 20°	FREE ACID MORE THAN 20°	TOTAL WITH FREE ACID	NUMBER	ACHLORHYDRIA	FREE ACID LESS THAN 20°	FREE ACID MORE THAN 20°	TOTAL WITH FREE ACID	NUMBER	ACHLORHYDRIA	FREE ACID LESS THAN 20°	FREE ACID MORE THAN 20°	TOTAL WITH FREE ACID	NUMBER	ACHLORHYDRIA	FREE ACID LESS THAN 20°	FREE ACID MORE THAN 20°	TOTAL WITH FREE ACID	NUMBER	ACHLORHYDRIA	FREE ACID LESS THAN 20°	FREE ACID MORE THAN 20°	TOTAL WITH FREE ACID
28-40	0					1	1				2	1		1	1	5	3	1	1	2	8	5	1	2	3
41-50	1	1				3	2		1	1	5	2	1	2	3	17	8	4	5	9	26	13	5	8	13
51-60	3	3				17	15	1	1	2	6	5		1	1	31	18	5	8	13	57	41	6	10	16
61-70	1	1				37	28	5	4	9	16	12	1	3	4	45	25	3	17	20	99	66	9	24	33
71-83	3	3				9	6	1	2	3	9	7	1	1	2	28	19	4	5	9	49	35	6	8	14
Total	8	8				67	52	7	8	15	38	27	3	8	11	126	73	17	36	53	239	160	27	52	79

tribution of the four types of tumor and the corresponding acidities according to age among 205 men. Table II shows the same data for 79 women. Table III combines the two sexes. Table IV shows the composite data for the 239 cases in which histamine had clearly been used as a test substance.

Examination of the tables reveals no real difference dependent on either age or sex and the incidences of anacidity are of comparable magnitude for the two sets of data relative to all acid determinations and those with verified histamine stimulation alone (Tables III and IV). The results can be conveniently summarized in terms of Table III, which includes all cases.

Of the 284 cases, 185 (65 per cent) showed achlorhydria, and 99 (35 per cent) showed free acid. Of these, 35 (12 per cent of the total) had maximum values of less than 20 degrees and 64 (22 per cent of the total) had maximum values of more than 20 degrees. The incidences of the acidities in each of the decades are quite comparable to that of the entire group.

There were 9 Type I tumors, all of which were associated with achlorhydria. These comprise 3.2 per cent of the total number and account for 5 per cent of the cases of achlorhydria.

There were 79 Type II tumors (27.8 per cent of the total), which provided for 57 (31 per cent) of the cases of achlorhydria. Twenty-two (28 per cent) of the Type II tumors were associated with free acid and thus accounted for 22 per cent of the total number of cases with free acid. Of these, 9 had less and 13 had more than 20 degrees.

There were 47 Type III tumors (16.5 per cent of the total), which accounted for 31 (17 per cent) of the cases with achlorhydria. Sixteen (34 per cent) of the Type III tumors were associated with free acid (16 per cent of the total cases that showed free acid) and, of these, 5 showed maximum values of less than 20 degrees and 11 showed more than 20 degrees.

There were 149 Type IV tumors (52.5 per cent of the total) and among these there were 88 (48 per cent) of the cases with achlorhydria. Sixty-one (41 per cent) of the 149 cases showed free acid (62 per cent of the total number of cases with free acid). Of these, 21 had maximum values of less than 20 degrees and 40 had more than 20 degrees.

The values for the cases in which histamine was certainly employed are of the same order of magnitude (Table IV). None of the Type I tumors, 22 per cent of the Type II tumors, 29 per cent of the Type III tumors, and 42 per cent of the Type IV tumors were found to be associated with free acid. Thus, 33 per cent of this series showed free acid in at least some degree.

COMMENT

In this series of cases only the tumors of Type I were constantly associated with achlorhydria and these comprise but 3.2 per cent of the group. With each of the other types of tumor a significant proportion of the cases showed free acid and, among these, the proportion was somewhat higher for tumors of Type IV than for Types II and III. Of the cases with free acid about one-third had values below 20 degrees, and two-thirds had values over 20 degrees.

This distribution is also approximated for each of the three types concerned. A further breakdown of the acidities in excess of 20 degrees show that of the 64 cases, 23 had maximum values between 20 and 30 degrees, and 41 had maximum values over 30 degrees. For the great majority of cases of gastric carcinoma there is no special relationship between achlorhydria or hypochlorhydria and a gross type of tumor.

Summarized differently, in this series of 284 cases, 243 (86 per cent) had achlorhydria or acid values below 30 degrees, 220 cases (77 per cent) had achlorhydria or acid values less than 20 degrees, and 185 cases (65 per cent) had achlorhydria. While these data follow others in showing the predominance of reduced secretory capacity, as of the time the diagnosis is made, in a group of cases of gastric carcinoma they also emphasize the fact that no range of acidity precludes the disease. Emphasis on the examination of individuals with achlorhydria or hypochlorhydria in order to detect most early gastric cancer is valid, however, only to the extent that achlorhydria with cancer also means achlorhydria before the cancer appears. The constancy of this relationship is established only in the case of pernicious anemia, though the study of Comfort, Kelsey, and Berkson[2] showed more achlorhydria and hypochlorhydria among patients who subsequently developed cancer than was normal for the ages concerned.

The character of the mucosa in these cases is to be considered in a separate report, but it may be noted here that for many there is an anatomic basis for anacidity as evidenced by complete loss of normal body glands. Such extensive atrophy may be found in association with tumors of any gross type, but it seems to be most consistently present with tumors of Type I. The group concerned is, of course, small but Dockerty[3] has called attention to a similar relationship. On the other hand, diffuse atrophy by no means necessarily accompanies gastric carcinoma (Hebbel)[4] and other patients in this series presented well-preserved body mucosas even though achlorhydria had been demonstrated. Here, achlorhydria is less readily explained. That histamine achlorhydria is not necessarily permanent is well known and perhaps, were repeated analyses to be performed, free acid might at some time be present in some such cases. Magnus[5] found no gastritis in the body mucosa in 22 of 25 cases of ulcerating carcinoma, and expressed the opinion that if achlorhydria precedes gastric carcinoma, it is not due to the loss of parietal cells.

SUMMARY

In a series of 284 cases of gastric carcinoma, 243 (86 per cent) had achlorhydria or maximum acid values below 30 degrees, 220 cases (77 per cent) had achlorhydria or maximum acid values below 20 degrees, and 185 cases (65 per cent) had achlorhydria. Achlorhydria was uniformly present only in association with tumors of Borrmann Type I and these totaled but 3.2 per cent of the series. For tumors of Borrmann Types II, III, and IV, there was no constant association of either achlorhydria or hypochlorhydria. Twenty-eight per cent of the Type II tumors, 34 per cent of the Type III tumors, and 41 per

cent of the Type IV tumors were associated with free acid on gastric analysis. In each of these groups the maximum acid values fell below 20 degrees in about one-third of the cases and exceeded 20 degrees in about two-thirds of the cases.

REFERENCES

1. Borrmann, R.: Das Wachstum und die Verbreitungswege des Magencarcinoms, Mitt. a.d. Grenzgeb. d. Med. u. Chir. (Suppl.) pp. 1-376, 1901.
2. Comfort, M. W., Kelsey, M. P., and Berkson, J.: Gastric Acidity Before and After the Development of Carcinoma of the Stomach, J. Nat. Cancer Inst. **7**: 367-373, 1947.
3. Dockerty, M. B.: Pathological Aspects of Carcinoma of the Stomach, in Collected Papers of the Mayo Clinic and the Mayo Foundation, vol. 38, Philadelphia, 1947, W. B. Saunders Company, pp. 19-24.
4. Hebbel, Robert: Chronic Gastritis, Its Relation to Gastric and Duodenal Ulcer and to Gastric Carcinoma, Am. J. Path. **19**: 43-71, 1943.
5. Magnus, H. A.: The Pathology of Simple Gastritis, J. Path. & Bact. **58**: 431, 1946.

CLINICAL STUDIES IN CRANIOSYNOSTOSIS

Analysis of Fifty Cases and Description of a Method of Surgical Treatment

Franc D. Ingraham, M.D., Eben Alexander, Jr., M.D., and
Donald D. Matson, M.D., Boston, Mass.

(From the Department of Surgery, Harvard Medical School and Neurosurgical Service, The Children's Hospital)

INTRODUCTION

THE striking and often grotesque deformities associated with premature closure of the cranial sutures have interested both physicians and laymen since antiquity. Descriptive names of Greek derivation, such as scaphocephaly, acrocephaly, turricephaly, and oxycephaly were used to designate these bizarre abnormalities of the head. With discovery of the roentgen ray, a more accurate clinical terminology based on physiologic and pathologic criteria became possible. Sear[1] and others, therefore, have recommended adoption of the term "craniosynostosis" to include all varieties of premature closure of the cranial sutures, adding to this diagnosis identification of the particular sutures involved in each instance. This terminology will be used in the present report.

The cranial sutures normally fuse long after the growth of the brain has been completed. Only the metopic suture normally closes at birth or shortly thereafter, the others remaining open until the age of 50 or 60 years. Bolk[2] has differentiated two phases in the surface growth of the cranial bones in infants. In the first phase, which extends into the second year of life, growth at the border of the membranous bones predominates. At the beginning of the second phase, the sutures become dentated and diffuse growth of the bones takes place at a slower rate. Extreme abnormality probably occurs only when synostosis begins during fetal life or shortly after birth, but lesser degrees of deformity are commonly seen when synostosis occurs within the first two years.

Craniosynostosis has been variously attributed to syphilis, rickets, prenatal or birth trauma, endocrine disorders, and meningitis.[3] There is little foundation for any of these theories and reviewing them would be of historical interest only. Patterson[4] in an unpublished review of Cushing's cases of *synostosis cranii* emphasized three facts which point to an inherent mesenchymal defect as the cause of premature closure of the sutures: first, there is a strong hereditary tendency, cases having been reported in two generations and several cases having occurred in siblings; second, associated congenital anomalies, particularly syndactylism, are commonly seen; and third, there is a greater incidence in males (85 per cent) than in females.

Many anatomic investigations of skulls showing craniosynostosis have been made, notable among which is the detailed study of oxycephaly by Greig.[5] Histologic studies through the suture lines and of the separate membranous bones of the skull have revealed nothing remarkable. The lack of any gross or

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microscopic abnormality in the bone itself has been confirmed by examination of many specimens removed at operation in the series of cases reported here. Likewise, there is no evidence that the actual growth and repair of membranous bone in these patients are impaired; in fact, it would appear that healing of bone occurs more rapidly in these patients than in normal patients.

A variety of apparently unrelated congenital anomalies has been described in association with premature closure of the cranial sutures. Park and Powers[3] reviewed twenty-eight cases of so-called acrocephaly in which there were varying degrees of syndactylism, a syndrome which has been termed acrocephalosyndactylism. Other anomalies including cleft palate, harelip, congenital heart disease, spina bifida, and meningocele, have been reported in association with craniosynostosis. Such anomalies apparently occur more frequently with this condition than in normal individuals.

Although the bony abnormalities in craniosynostosis are important, because of the grossly deformed heads which may result, of much greater significance is the compression of the growing brain which occurs secondary to this premature bony fusion. The relation of premature closure of the cranial sutures to mental development has often been misinterpreted, principally because of confusion of this condition with true microcephaly. Because of the vast difference in treatment and in prognosis, the fundamental difference between these conditions should be clearly understood. In microcephaly, the primary difficulty is failure of the brain to grow. The cranial sutures are present, but the head does not expand because there is no growth pressure from within. In craniosynostosis growth of the brain is normal, except as it is restricted by the limitations of the prematurely fused cranial sutures. In microcephaly, decompressive procedures are of no avail in the prevention or treatment of cerebral deficiency. In craniosynostosis, on the contrary, early prophylactic decompression which permits expansion of the brain to approximate a normal rate should allow mental development to proceed uninhibited.

Scammon and Dunn,[6] and Coppoletta and Wolbach[7] have determined that the brain increases about 85 per cent in weight in the first six months and 135 per cent in the first year of life (Fig. 1). After the second year, growth is slower but still rapid, and after the eighth year relatively little increase in brain bulk occurs.

The clinical implication of these observations is readily apparent; namely, the earlier the onset of premature craniosynostosis, the more likely is damage to ensue. Conversely, the earlier premature closure of the sutures is recognized and alleviated by surgical treatment, the less likelihood there is of subsequent cerebral deficiency.

Faber and Towne[8] were the first to stress the importance of early surgical treatment to prevent mental retardation and visual impairment. The purpose of the present report is twofold: first of all, to present clinical studies of fifty cases of premature craniosynostosis seen at the Children's Hospital and to re-emphasize the importance of diagnosis and treatment in the first months

of life, and second, to describe a method of surgical treatment in this age group. The historical development of therapy for premature craniosynostosis, as well as the signs, symptoms, classification, roentgenologic findings, and the diagnosis have been reviewed recently by Simmons and Peyton[9] and will be discussed here only in brief.

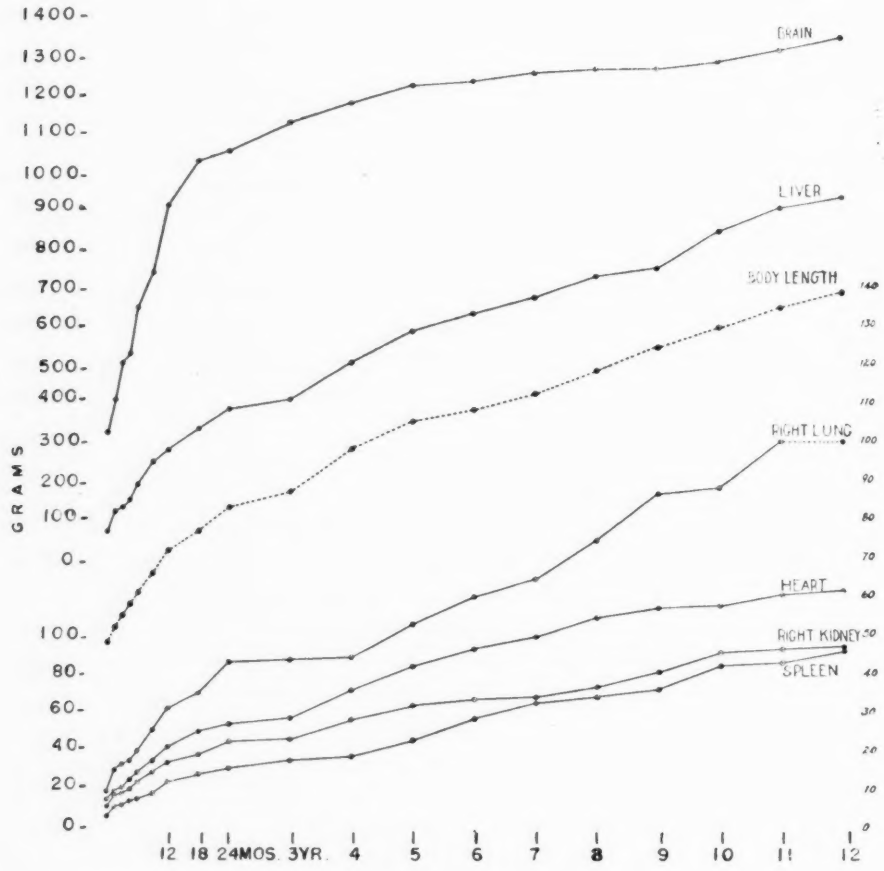


Fig. 1.—Chart showing rapid increase in brain weight in first two years compared to other organs of the body. Growth of the brain is much slower after two years. (After Coppoletta and Wolbach: Am. J. Path. 1933.[7])

ANALYSIS OF CASES

Virchow[10] recognized that when one or more of the cranial sutures closes before the rapid growth of the brain is completed, the skull expands in a direction axial to the closed suture. Thus when the sagittal suture closes prematurely, the coronal and lambdoid sutures permit greater anteroposterior expansion than would normally occur. The skull, therefore, becomes elongated, or scaphocephalic. Similarly, if the coronal suture alone closes prematurely, the patent sagittal and squamosal sutures permit added lateral growth and the forehead becomes prominent and wide, or acrocephalic. When closure of the coronal, sagittal, and lambdoid sutures occurs prematurely, the head can

expand only upward at the anterior fontanel. To this type of deformity the term oxycephaly has commonly been given. The base of the skull becomes deepened, the sinuses obliterated, and the orbits shallow. The head is small and narrow at its vertex. There may also be synostosis between the facial bones resulting in severe distortion of the face.

The cases in the present series fall into four main groups: (1) those in which the sagittal suture alone is closed; (2) those in which the coronal suture has closed; (3) those in which two sutures have closed; and (4) those in which all of the sutures have closed. The clinical picture and course, the prognosis, and the operative treatment vary in each group, although the fundamental pathology is the same. Rarer miscellaneous types of craniosynostosis will be mentioned briefly, after considering each of the four main groups separately.

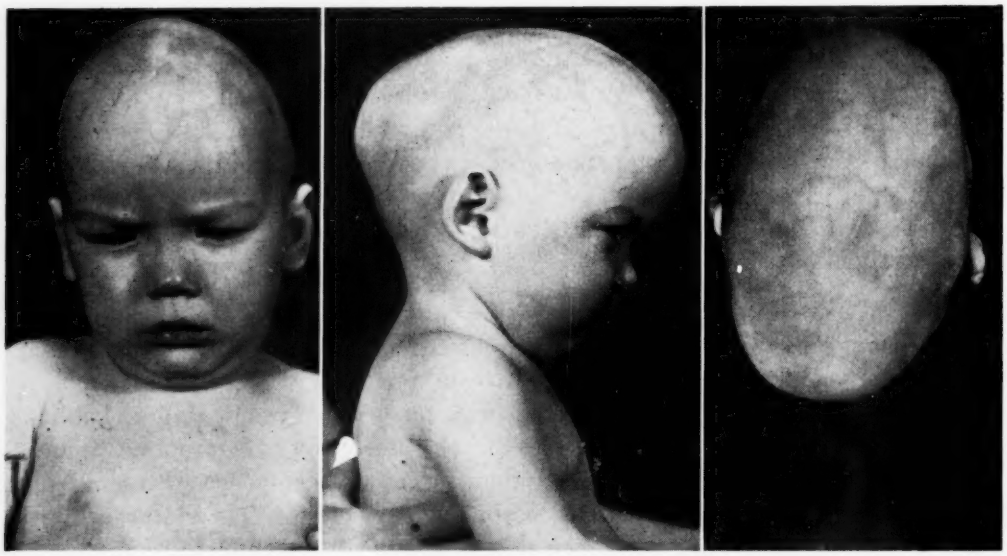
Premature Closure of Sagittal Suture.—In the present series, there have been twenty-nine cases of premature closure of the sagittal suture. Of these, twenty-four were in males and five in females. Of the twenty-nine, a total of nine cases have been found with associated congential anomalies. These included an ectopic right kidney, congenital hypertrophic pyloric stenosis, a *cavum septi pellucidi* shown in a pneumoencephalogram, a hemangioma of the thigh, a mild hypospadias, a cholesteatoma of the skull, a congenital dislocation of the cervical spine, as well as clubhands and clubfeet, webbed toes, syndactylism of both hands and feet, and cartilaginous inclusions of both humeri.

There were seven definitely retarded children. One of these, a girl, was operated upon at the age of 8 months. A pneumoencephalogram showed marked atrophy of the cerebral cortex. Right subtemporal decompression and parasagittal craniectomies failed to bring about any improvement and the patient showed, at the age of 3 years, 8 months, evidence of severe retardation. Five of the other children showing evidence of retardation before operation have presented a slightly more optimistic picture. They were first operated upon at 17 months, 19 months, 24 months, 25 months, and 8 years, respectively. In three of this group, there was felt to be definite improvement after operation, though evidence of retardation persisted; the fourth has been followed for too short an interval to permit reliable observation; one patient was not operated upon.

Ocular difficulties have rarely been seen associated with premature closure of the sagittal suture. One patient showed mild exophthalmos without apparent disturbance in vision; another patient treated at the age of 1 year by bilateral subtemporal decompression was reported to have diminution of vision in one eye and a marked strabismus.

Four patients in this group have had pneumoencephalograms. In one, there was evidence of severe cerebral degeneration which it was felt occurred coincidentally with synostosis rather than as a result of it. In the other three cases, the question of mental retardation was raised and pneumoencephalograms were done to aid in evaluation. In each instance, the deviation from normal in the pneumoencephalogram was slight. One of these children, who

showed slight dilatation of one lateral ventricle, has been followed to the age of 15 years and is on the honor roll in school. The other two children who showed slight ventricular dilatation are now normal or only slightly retarded.



A. *B.* *C.*

Fig. 2 (Case 19).—*A*, *B*, and *C*, Premature closure of sagittal suture; the head is elongated and narrow.

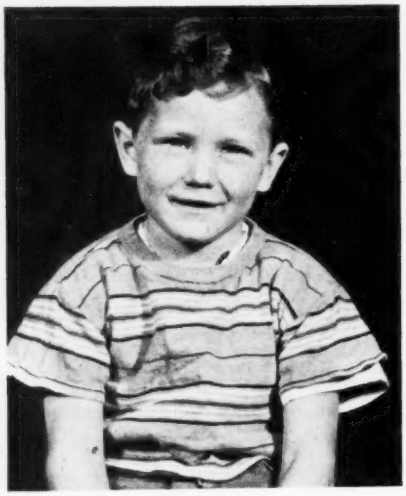


Fig. 3 (Case 5).—Brother of another patient (Case 19). These siblings showed premature closure of sagittal suture at birth. This patient, the older brother, was operated on as an infant. He is now, at the age of 10 years, normal in every respect.

Fifty-five per cent of the patients have been operated upon in the first year of life. Of the last eleven, all of whom have come to the Neurosurgical Clinic in the past year, only four have been over 1 year of age. All were under 2 years (Figs. 2 and 3).

Patients who present the characteristic deformity at birth of scaphocephaly and are operated upon in the first few weeks of life show a striking change in contour of the head (Fig. 4). Patients operated upon after the age of 10 to 12 months are less likely to show change in skull contour but frequently show more marked clinical improvement since the cerebral hemispheres of these children have undergone deformity over a longer period of time. Children operated upon after the age of 2 years show little immediate

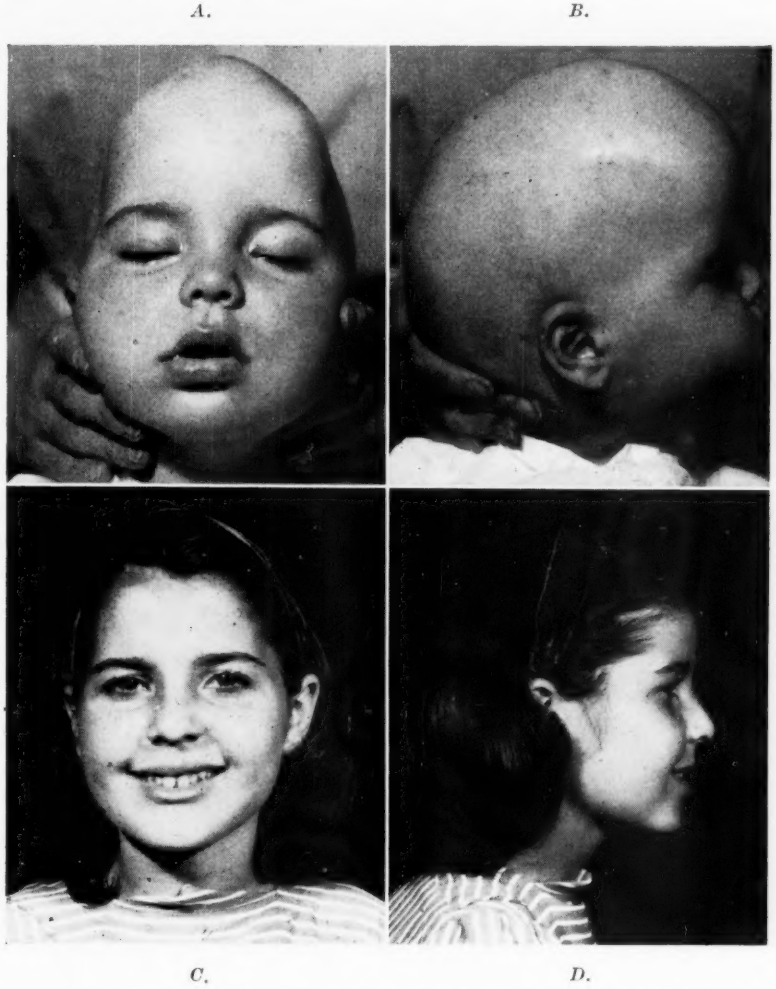


Fig. 4 (Case 3).—*A* and *B*, Upper photographs show patient as an infant before operation, at which time she was considered to be retarded. She was operated upon soon after this photograph was taken. *C* and *D*, Lower photographs show patient at the age of 12 years.

alteration in skull shape but again the clinical improvement may be impressive. A striking example of alteration of the shape of the cranial cavity is evident in the illustration of Case 23 (Fig. 5). The deformity of the infant's head was noticed at birth, the diagnosis confirmed by roentgenography within the first two weeks, and the patient operated upon at the age of 5 months. The postoperative photographs taken at the age of seven months show the striking change toward normal.

Of the twenty-nine cases in this group, twenty-seven patients have been operated upon. Since 1935 several types of operations have been used, including subtemporal decompressions and multiple linear craniectomies. Bilateral parasagittal craniectomy has proved to be the operation of choice for premature closure of the sagittal suture. Mount[11] has performed a

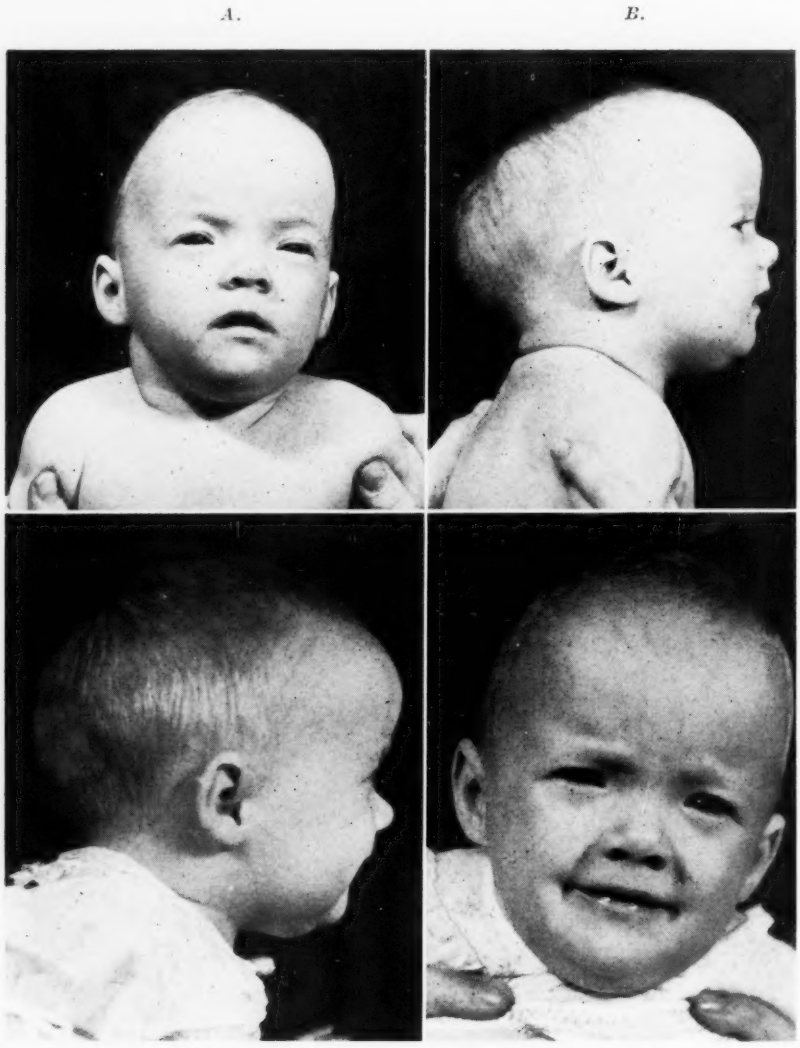


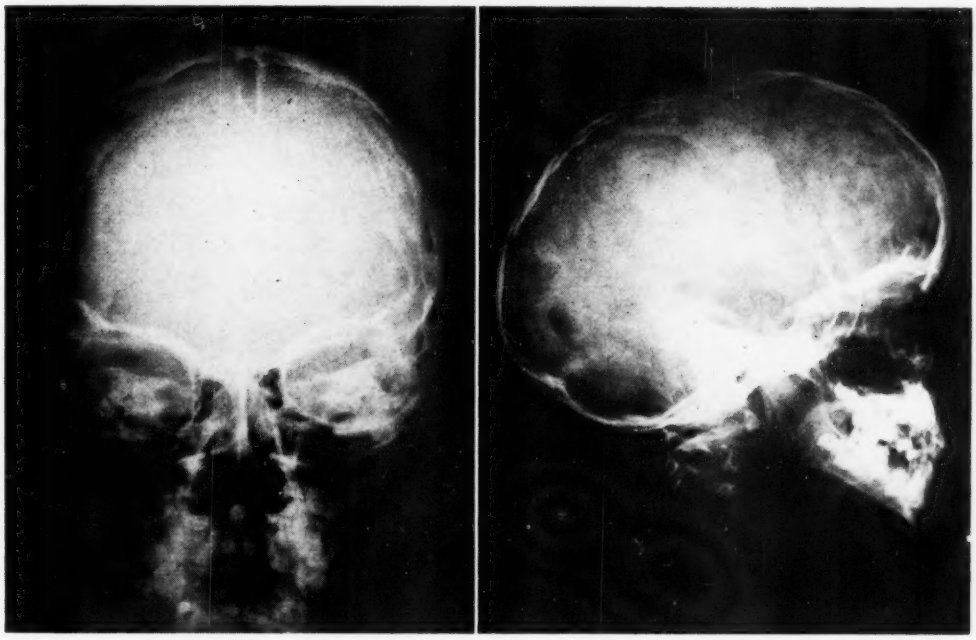
Fig. 5 (Case 23).—*A*, *B*, *C*, and *D*, Pre- and postoperative photographs of patient with premature closure of sagittal suture. Postoperative photographs show normal contour of head two and one-half months after bilateral parasagittal craniectomies performed at the age of 5 months.

midline sagittal craniectomy in cases of this type but such a procedure endangers the sagittal sinus, both at the time of operation and during the postoperative period. In this series, a strip of bone in the midline has been left for the protection of the sinus.

An illustrative case from this group is outlined here.

CASE REPORT.—C. E. D. (Fig. 6) was first admitted to The Children's Hospital with right upper lobe pneumonia at the age of 9 months. At that time the anterior and posterior fontanels were closed and the head was elongated with prominence of the frontal region. Roentgenographic examination of the skull at the age of 15 months showed the sagittal suture to be fused. The patient developed normally to the age of 4 years and was not referred for surgical treatment. Between the age of 4 and 6 years he became very irritable and uncooperative. He constituted a distinct behavior problem in his home and developed enuresis, a symptom he had not displayed previously.

In July, 1938, he was first referred to the Neurosurgical Clinic. He was a well-developed and nourished boy who was very uncooperative. Complete physical and neurological examinations were normal. There was no papilledema. Laboratory studies of blood and urine showed no abnormalities. A pneumoencephalogram showed moderate dilatation of the left lateral ventricle and no other abnormalities.



A. *B.*

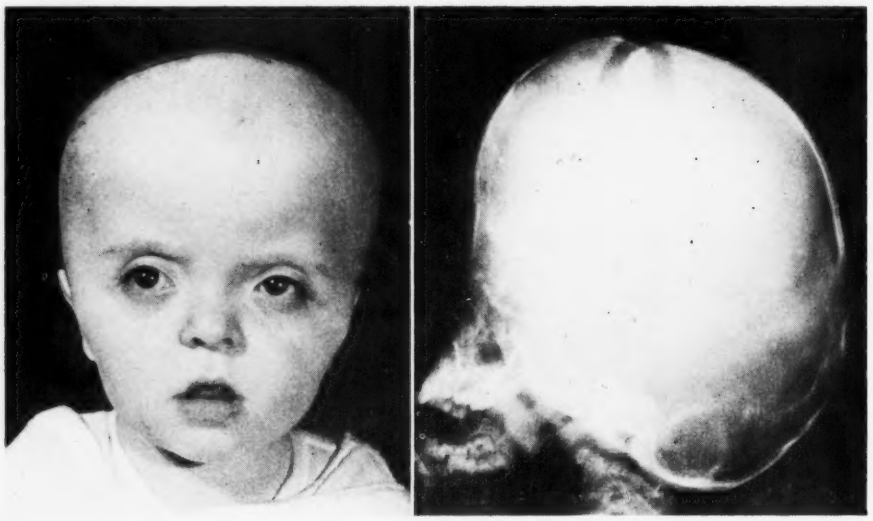
Fig. 6 (Case 1).—*A* and *B*, Roentgenograms of patient, aged 6 years, with craniosynostosis of sagittal suture. Behavior problem was greatly improved by operation. He was on honor roll in school at age of 14 years. Note fusion of sagittal suture and slight increase in convolutional markings of skull.

Bilateral subtemporal decompressions were performed in July, 1938. He was seen one month after discharge from the hospital, at which time his mother stated that she and her neighbors were amazed by his personality improvement. At the age of 11 years he was doing well in the fifth grade. He was last seen on July 18, 1946, at the age of 14 years. He showed no signs of pressure, the decompressions were still open and soft, and he was noted to be on the honor roll in school.

Premature Closure of Coronal Suture.—Premature closure of the coronal suture alone presents a striking contrast to closure of the sagittal suture. The anterior portion of the head becomes high and broad. There is frequently gross deformity of the forehead, occasionally hypertelorism and ptosis of the eyelids. Asymmetry is commonly seen in those cases in which the closure

occurs after birth, since one coronal suture may fuse completely before the other.

In the present series there were eight patients with premature closure of the coronal suture, five females and three males. Three of these children showed evidence of mental retardation to objective psychometric examination.



A. *B.*

C. *D.*

Fig. 7 (Case 34).—*A*, *B*, *C*, and *D*, Patient with premature fusion of coronal suture and syndactylism of hands and feet. The characteristic deformity of the head and the healed incision of a recent bilateral coronal craniectomy are evident. Lateral roentgenogram of skull shows deformity of head ten days after operation.

In spite of the striking deformity in this group, only one patient reached the hospital for operation at the age of 6 months and only three under 1 year. None of these patients showed evidence of increased intracranial pressure.

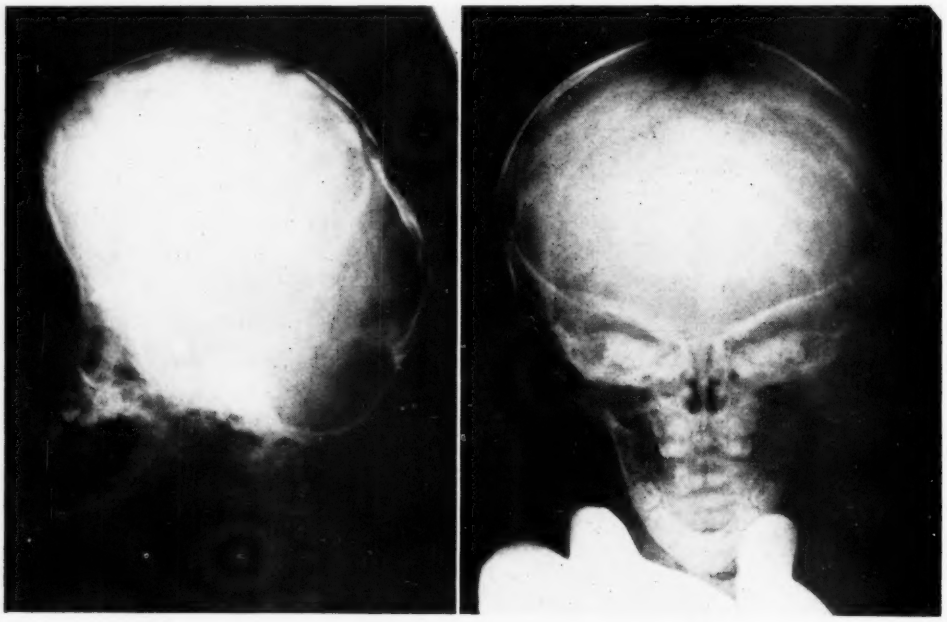
The incidence of associated congenital anomalies in these cases has been high: in the first case, persistent enlarged parietal foramina of the skull; in the second, large parietal bone defects and bifid uvula; and in four others

syndactylism of all four extremities (Fig. 7). If strabismus, ptosis, and exophthalmos were present before operation, they seemed to improve slowly months or years after operation (Figs. 8 and 9).

Fig. 8 (Case 30).—*A*, *B*, *C*, and *D*, Pre- and postoperative photographs of patient with premature closure of coronal suture. At the age of 9½ years she has normal intelligence and appearance has improved as the years have passed. Younger brother of this girl also had craniosynostosis of coronal suture.

Surgical treatment in these cases has consisted of coronal craniectomy either in one or two stages, removing a 1.0 cm. strip of bone extending from one squamosal suture across the midline to the other. In three cases, bilateral subtemporal decompressions were also performed. One patient had coronal craniectomy repeated two years after the original operation, which was performed at the age of 6 months.

Most of the children in this group have been operated upon at a relatively late age and in none of them has there been a striking change in the shape of the head within a few weeks of operation. The one child in this series who has been followed to the age of 9½ years has shown improvement in the contour of the head and has developed normally. Earlier operation, that is, in the first two or three months of life, should do much to improve the gross cranial deformity evident in all of these children.



A. *B.*

Fig. 9 (Case 30).—*A* and *B*, Anteroposterior and lateral roentgenograms of skull show wide transverse diameter typical of premature closure of the coronal suture. The forehead is high and the head brachycephalic.

Premature Closure of Two or More Sutures.—

Premature closure of sagittal and coronal sutures: Four children were seen in whom there was premature closure of the sagittal and coronal sutures, the other cranial sutures being patent. One of these showed an additional deformity characteristic of fusion of the metopic suture, a very pointed forehead. Operation was carried out at the age of 3 months and when last seen, at the age of 8 months, there was improvement in head shape, as well as apparently normal mental development. In constrast to the first patient, a second child came to the hospital for operation at the age of 5½ years. The sequence of closure of her cranial sutures is not known but the forehead was broad and high. There was also asymmetry of the head, presumably due to closure of one side of the coronal suture before the other. The deformity in both of these children was that of a brachycephalic head with increase in height of the forehead. The third patient was seen only once in the hospital because of "peculiar deformity" of the head at the age of 12 years. Roentgenograms

showed closure of the coronal and sagittal sutures and admission to the hospital was advised but refused. The roentgenograms in this instance also showed a very high forehead and a brachycephalic skull with accentuation of digital markings. At the age of 22 this patient was reported to be in the United States Navy. Only one patient in this group exhibited any other anomaly. That child had bilateral syndactylism of hands and feet.

Two of these patients have had primary operations too recently to determine final results and a third had no operation. The fourth patient showed no retardation before operation at the age of 4½ years and has continued to develop normally. The youngest child showed papilledema bilaterally before operation and this was relieved by operation. None of these children has shown distinct evidence of retardation and it can only be surmised that this combination of suture closure is a serious one but does not carry with it as ominous a prognosis as other combinations to be discussed here.

Premature closure of sagittal and lambdoid sutures: In the experience of The Children's Hospital, there have been three patients with premature closure of the sagittal and lambdoid sutures. Each of these showed evidence of obvious mental retardation when first seen in the hospital. One of these, first operated upon at the age of 23 months, has improved and is considered by her family to be bright, but objective psychometric examination showed significant retardation. The other two patients, first treated surgically at the age of approximately 3 years, have shown no real improvement and were retarded mentally when last seen. This group of cases showed frequent association of other congenital anomalies. One child had multiple congenital anomalies of the vertebrae, another had exophthalmos and strabismus, which were not secondary to increased intracranial pressure.

Surgical treatment in each of these children included linear craniectomies and subtemporal decompressions, none of the procedures being done earlier than the age of 23 months. Pneumoencephalograms in two of these patients showed gross ventricular dilatation and cortical atrophy.

It is of some interest that in two of the three patients of this group, the coronal suture was distinctly open at the age of approximately 3 years. At the age of 4, in one case and 7 in the other, there was roentgenographic evidence of closure of all of the cranial sutures. The third patient showed some progression toward complete closure of all sutures at the age of 2 years. It is obvious, therefore, that these three patients, if seen for the first time at more advanced ages, would have been included in the oxycephalic group with complete closure of all cranial sutures.

Premature Closure of All Cranial Sutures.—Patients with premature closure of all the cranial sutures present a reasonably consistent deformity of the head but the contour may vary slightly depending on the sequence in which the sutures fuse. The head is usually small, pointed at the vertex, with the eyes prominent. Greig[5] divided such cases into true oxycephaly and delayed

oxycephaly. In the first group, the closure of sutures is present at birth. In the latter, it develops sometime in the postnatal period or in later infancy or childhood.

According to previous reports in the literature, these children have commonly shown not only mental deficiency but blindness as well. Many explanations of the blindness associated with synostosis of all the sutures have been suggested, the most reasonable being that optic atrophy results from chronically increased intracranial pressure. Most writers have agreed that if blindness does not develop before the age of 8 years, it rarely appears.

This series includes six patients with clinical and roentgenologic evidence of closure of all the cranial sutures. One of these patients was operated upon first at the age of 3½ months, one at 4 years, eleven months, one at 5 years, one at 6 years, and one at 7½ years. Only one of these patients showed any associated congenital anomaly. That child first had a roentgenogram taken at the age of 7½ years and showed fusion of all sutures. Her head contour is typical of those cases with closure of the coronal suture. She had syndactylism of hands and feet.

On admission to the hospital, the two youngest patients showed definite papilledema bilaterally. Both of these showed complete remission of the papilledema after decompressive operation. The other three patients, all seen after they were 5 years of age, had various degrees of optic atrophy but no demonstrable loss of visual acuity. None of these has shown any progression of visual disturbance and it seems fair to assume that surgical procedures were effective in preventing any further loss of vision. All of this group showed accentuation of digital markings in the skull by roentgenographic examination (Fig. 10).

The type of surgical treatment carried out has varied as experience has increased. In three of the earlier patients, subtemporal decompressions combined with linear craniectomies were done. In the last two, linear craniectomies were performed without subtemporal decompressions. The three older patients of this group were obviously retarded mentally on admission to the hospital. One of them showed no significant improvement after operation; the other two were considered improved postoperatively by their families, but were nevertheless retarded. One is slightly retarded with an I. Q. of 99.

The fourth patient first showed closure of the coronal and sagittal sutures at the age of about 18 months, but at that time there was no evidence of increased intracranial pressure, no mental retardation, and no visual disturbance. During the fourth year, his mental development became noticeably retarded and there was bilateral papilledema. Subtemporal decompressions were performed. Subsequently coronal craniectomy was also done and the latter operation was repeated three years later. The patient has recently been seen at the age of 11 years and, although small for his age, he is not mentally retarded and has adequate, if not completely normal vision (Fig. 11).

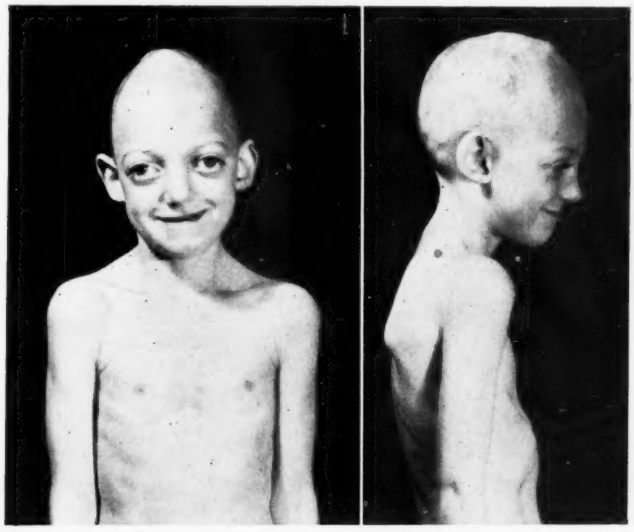
A report of the youngest patient in this group is presented in some detail (Fig. 12).

CASE REPORT.—R. C., a male infant, was 3½ months old when first admitted to the hospital. Birth weight was 4 pounds, 12 ounces. Closure of the sutures had been noted at birth and confirmed by roentgenogram at 5 days of age. After birth the infant gained weight slowly and had repeated cyanotic attacks, particularly after feedings. The patient was beginning to hold up his head and to recognize objects, at the age of 3½ months.

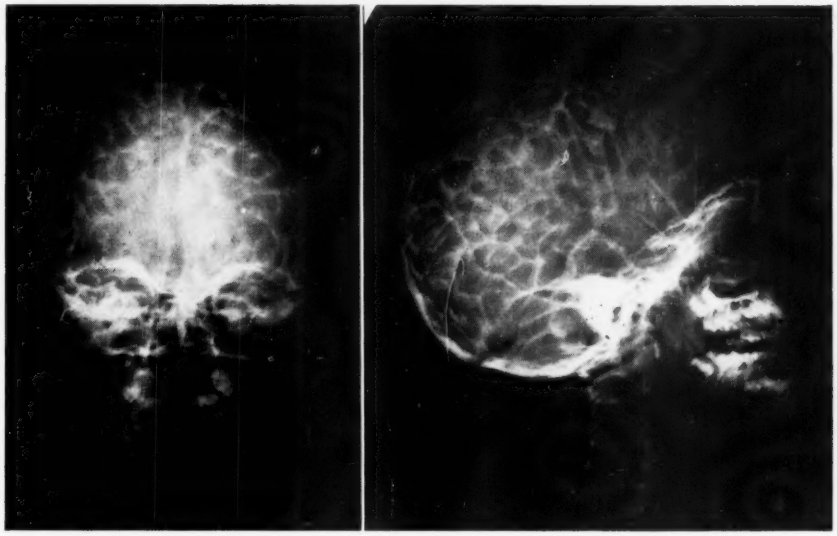
Family history was noncontributory.

Physical examination revealed temperature, 98° F.; pulse, 120; respirations, 30; blood pressure 100/65.

The head measured 38.5 cm., forehead and vertex narrow. The head tapered toward the midline in the posterior parietal region. The veins of the scalp were dilated and the skin



A. *B.*

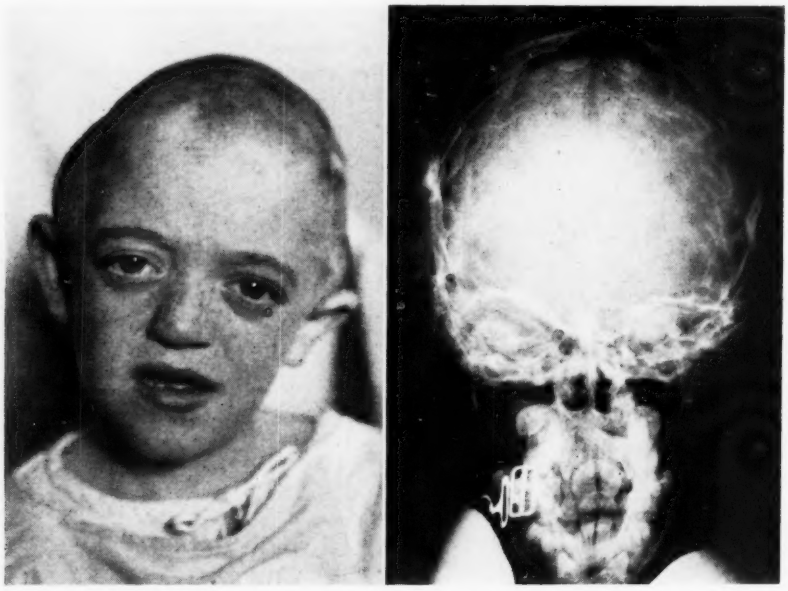


C. *D.*

Fig. 10 (Case 46).—*A*, *B*, *C*, and *D*, Premature closure of all cranial sutures. Roentgenograms show small head, absence of sutures, accentuation of digital impressions, and obliteration of accessory sinuses.

was very red. The fontanels were closed. The eyes were prominent but there was no definite exophthalmos. The optic discs showed papilledema of 1 to 2 diopters. There was noisy breathing through the nose and mouth but no organic obstruction was found. There was a systolic murmur over the precordium and a questionably enlarged heart. The remainder of the examination was normal.

During the patient's course in the hospital there was choking, respiratory obstruction, and transitory cyanosis on repeated occasions during feedings.

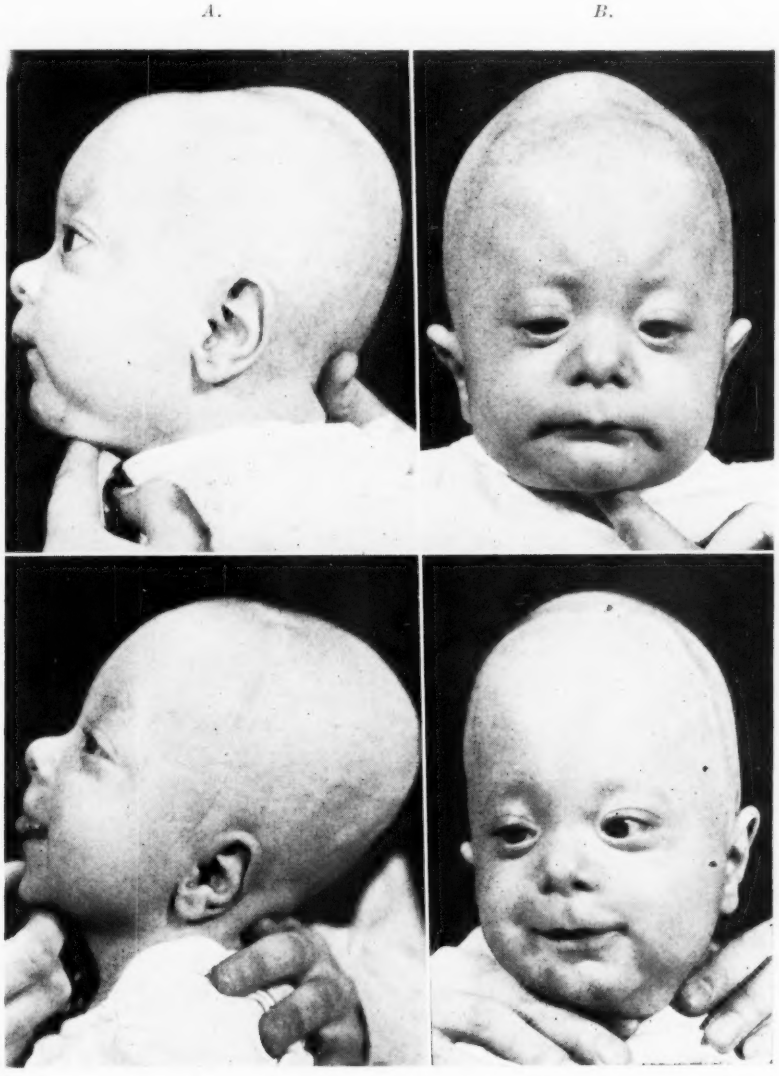


A. *B.*

C. *D.*

Fig. 11 (Case 47).—*A*, *B*, *C*, and *D*, A patient with premature closure of coronal and sagittal sutures treated by bilateral subtemporal decompression. Roentgenogram shows bulging of decompression on right with bone regenerating over surface. Photograph taken after left side had also been operated upon. Coronal craniectomies later performed. Patient has normal intelligence at the age of 11½ years.

Operations were performed at the age of 3½ months. On two occasions Avertin, 100 mg. per kilogram, was administered per rectum but on each occasion the child became cyanotic, showed Cheyne-Stokes respirations and apnea, and required artificial respiration. Drop ether had the same general effect. On a third occasion brandy was administered by stomach tube and a coronal craniectomy was carried out under local procaine anesthesia. In a similar manner a lambdoid craniectomy was done eleven days later. Polyethylene film was inserted over the bone edges of the craniectomies.



A. *B.*

C. *D.*

Fig. 12 (Case 45).—*A*, *B*, *C*, and *D*, Pre- and postoperative photographs of an infant with premature closure of all cranial sutures. Preoperative vascular congestion, papilledema, cyanotic attacks, and mild exophthalmos relieved by coronal and lambdoid craniectomies.

Postoperatively the patient did extraordinarily well. There were no further cyanotic attacks and the noisy respiratory sounds became less marked and finally disappeared. The head showed rapid enlargement with spreading of the artificial sutures, particularly of the coronal. Physical and mental development progressed normally, the papilledema disappeared, and vision was grossly normal.

At the age of 8 months the child developed a severe respiratory infection and died of an overwhelming pneumonia twenty-four hours later. Post-mortem examination showed pneumonia to be the cause of death. The bronchial tree and the cardiovascular system were free of congenital anomalies. The head showed the coronal craniectomy to be 4 to 5 cm. in width compared to its original width of 1 cm. There was no increased intracranial pressure. There was a mild degree of platybasia. It was of particular interest that the brain weighed slightly more than normal for the age of the patient and serial coronal sections showed no abnormalities.

There was no evident foreign body reaction to the polyethylene film over the bone edges of the craniectomies. New bone had re-formed from the periosteum and had attempted to grow over the layer of film to close the defect in the skull.

Other Types of Synostosis Cranii.—Occasionally patients are seen in whom one side of the coronal suture only has closed, leaving all of the other sutures patent. This results in an asymmetry of the head which has been termed plagiocephaly (Fig. 13)). In the experience of this clinic, such mild deformities have not interfered with the normal growth of the brain and it has not been

Fig. 13 (Case 39).—Premature closure of one coronal suture in an infant giving an asymmetrical forehead. This patient later developed premature closure of both sides of the coronal suture and of the sagittal suture, requiring operation.

necessary so far to treat such patients surgically. It is of extreme importance, however, to follow these patients closely with periodic physical and roentgenographic examinations because closure of one-half of the coronal suture may be the precursor of closure of the other half or of closure of the sagittal suture, a sequence of events which probably occurred in one of the patients discussed previously.

More frequently than plagiocephaly, one sees normal children with markedly pointed foreheads. This deformity, called trigonocephaly, is the result of premature closure of the metopic suture. Normally this suture is obliterated at the time of birth, although it may persist for months or years. In order to cause deformity of this type, closure of the metopic suture must occur in utero (Fig. 14).

This deformity has been found to be of no clinical significance so long as the other suture lines are normal and it has been felt that no surgical treatment is necessary except when the deformity is so marked as to warrant surgery for the cosmetic effect.

SURGICAL TREATMENT

It has been the experience of most neurosurgeons that any decompressive operation performed in infants for *synostosis cranii* is effective for a relatively short time because of the tendency of the bone to heal rapidly. Reports by King,[12] Woodhall,[13] Faber and Towne,[8] and others have indicated that to gross palpation and to roentgen-ray visualization, operative skull defects often show firm healing in four months. Judging from the experience at The Children's Hospital, it is doubtful if simple linear craniectomies performed in infants permit expansion of the skull longer than four to eight months. Cases have been observed in which 1 cm. strips of bone have been removed from each parasagittal region; roentgenograms taken twelve months later showed complete healing with almost no evidence of the previous craniectomies. Others have shown solid bone bridges across the craniectomies within six months, thus preventing further skull expansion.

A. *B.*

Fig. 14.—*A* and *B*, Characteristic deformity of premature closure of the metopic suture. This deformity ordinarily requires no surgical treatment.

Many types of operations for the relief of craniosynostosis have been described since Lannelongue[14] in France in 1890 and Lane[15] in the United States in 1892 first used linear craniectomies for the relief of craniosynostosis. Subtemporal decompressions have been used widely during the past forty years and apparently with some success. Numerous other techniques have had their proponents, but there is a growing feeling that linear craniectomy in the region of the fused sutures is the most physiologic method for allowing a crowded or deformed brain to grow in normal fashion.

While any one of several types of craniectomy produces satisfactory immediate relief of cerebral compression in older children, all of the methods previously reported have been inadequate for treatment of premature craniosynostosis in early infancy. The rapid rate of bone regeneration in this age group has resulted in reclosure of artificially created sutures or decompressions before the period of rapid brain growth has been completed. This has necessitated secondary operations frequently in the series of cases treated at The Children's Hospital. Of fourteen patients under 2 years of age treated by linear craniectomy and followed for more than one year, eight have required secondary procedures because of bony fusion of the craniectomies.

Experimental studies were therefore instituted in the laboratory to discover methods suitable for use in infants to prevent or retard significantly the healing of artificial suture lines. These experiments have been reported by Ingraham, Matson, and Alexander.[16] It was found that certain inert foreign materials, including tantalum, methyl methacrylate (Lucite), and polyethylene will significantly retard the healing of artificial cranial sutures in young animals. Of these three materials, polyethylene in the form of a thin film is the easiest to handle technically and is least expensive; it has therefore been adopted routinely for use over the cut edge of artificially created cranial sutures in patients. Since this experimental work was completed, Simmons and Peyton[9] have reported the use of tantalum foil over one margin of artifically created sutures in two infants with craniosynostosis.

Present Technique.—For premature closure of the coronal suture, a coronal craniectomy is performed, extending from one squamosal suture across the vertex to the other. Lambdoid craniectomy is similarly done for premature closure of that suture. For sagittal suture closure, parasagittal craniectomies are performed, leaving a strip of bone 3 cm. in width in the midline over the sagittal sinus. These craniectomies should always extend beyond the lambdoid and coronal sutures. The operations are performed under ether anesthesia.

Although new bone forms from the dura, which is the endosteum, the periosteum re-forms bone much more rapidly. The only significant bridges across skull defects in the laboratory animals were seen on the external surface, having regenerated from periosteum. This has led to a wide removal of periosteum adjacent to craniectomies in patients. After opening the scalp, therefore, the pericranium is resected for a distance of 2 to 3 cm. on each side of the proposed craniectomy.

A linear craniectomy is performed by making multiple burr holes 5 to 7 cm. apart either at the site of the synostosed suture or adjacent to it. These burr holes are connected by a Gigli saw, removing strips of bone 1.0 to 1.5 cm. in width. The burr holes may be connected by scissors in infants under 4 to 6 months of age. The dura is not opened but it is separated from the bone about 1.5 cm. to either side of the linear craniectomy. Drill or punch holes 2 mm. in diameter are made 6 mm. back from each bone edge at intervals of 5 cm.

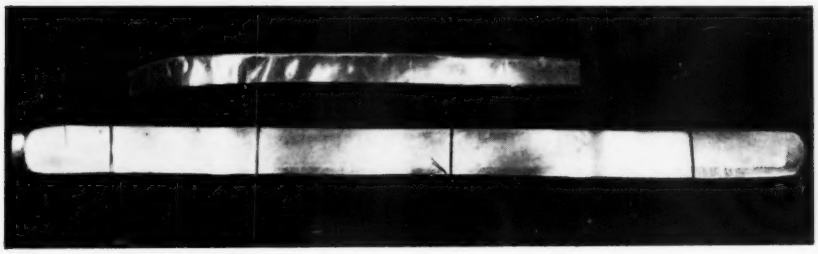


Fig. 15.—Polyethylene film folded over curved malleable retractor prior to sterilization by boiling. It retains the curved contour which facilitates the insertion of the film over the bone edges. At the top, the film has been removed from the metal retractor.

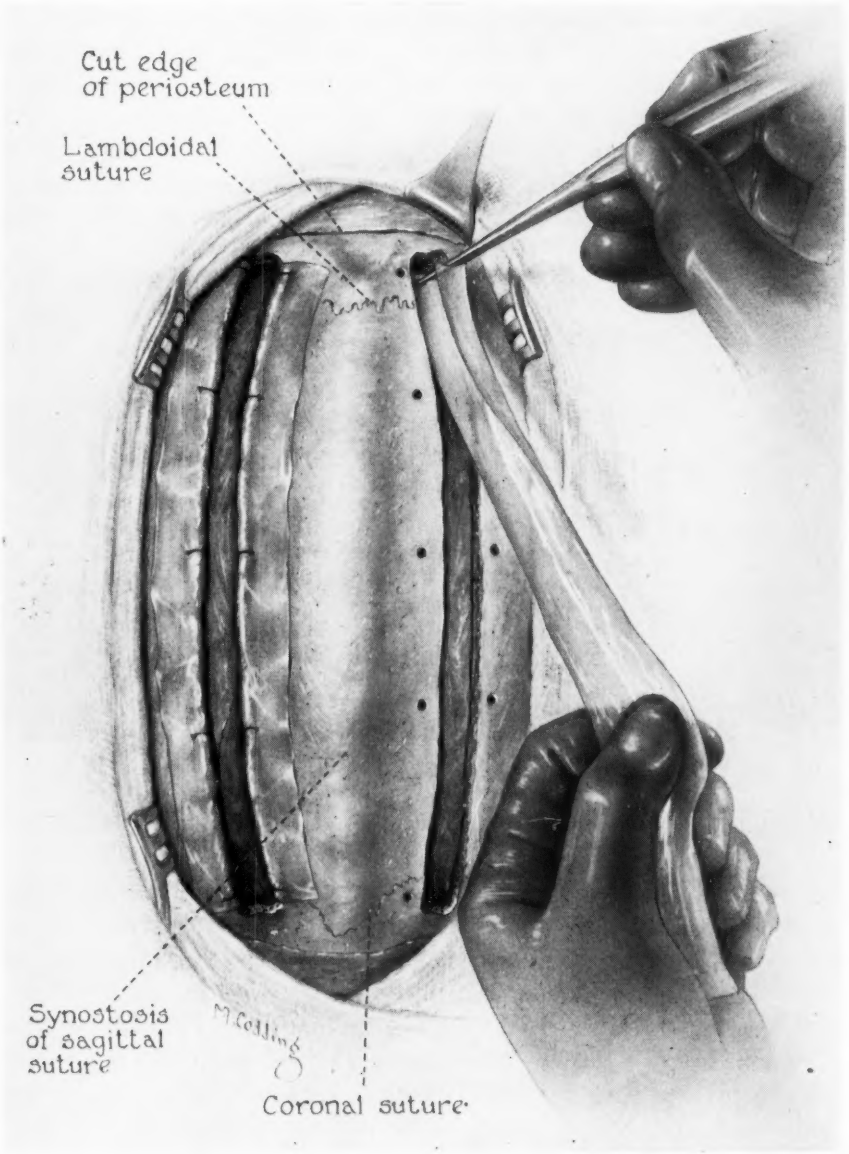
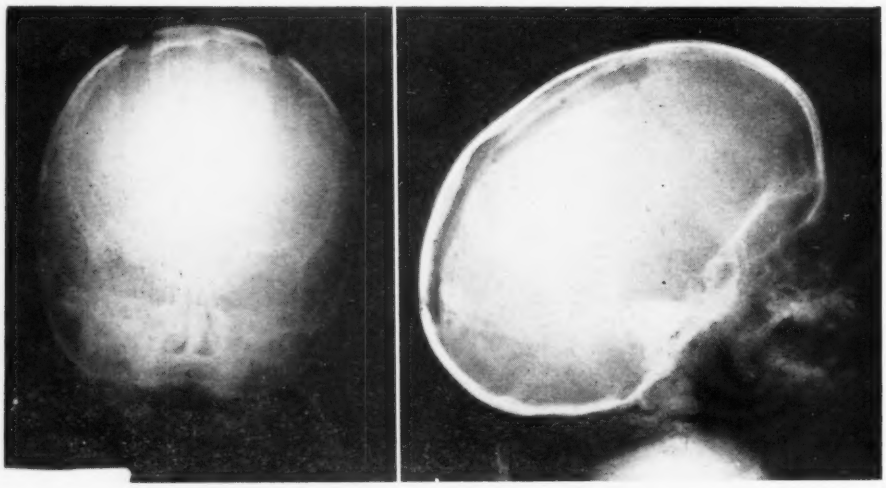


Fig. 16.—Operative field in a case of premature closure of the sagittal suture. Parasagittal craniectomies have been done, the periosteum widely resected. Polyethylene film has been inserted on one side and is being fixed in position on the other side.

Polyethylene film 0.005 cm. thick is cut in strips 2.5 cm. wide and about 25 cm. long.* It is folded over the edge of a malleable abdominal retractor bent according to the contour of the infant's head. The folded film is held in position with tape or large caliber string pulled firmly but not tightly (Fig. 15). The malleable retractor and the film are wrapped in a gauze sponge and boiled in water for thirty minutes. Autoclaving will change the plastic film into an amorphous mass, but boiling alters the film only in making it maintain the U-shape it assumed during the boiling process.

A piece of the sterile U-shaped polyethylene film is then trimmed so that each limb is about 1.0 cm. wide and the length conforms exactly to the length of the craniectomy. It is inserted over the margins of the craniectomy and held in place by silk sutures passed through the drill holes and the film (Fig. 16). The film tears only with strong force. It can be handled easily, therefore, and with a little experience made to lie smoothly over inner and outer bone surfaces. The film is placed over both edges of each craniectomy. The scalp wound is then closed in layers with interrupted sutures of fine silk.



A. *B.*

Fig. 17 (Case 27).—*A* and *B*, Anteroposterior and lateral roentgenograms ten days after bilateral parasagittal craniectomy in an infant. Characteristic deformity of premature closure of the sagittal suture is evident. Craniectomies carried through coronal and lambdoidal sutures.

Twenty-two linear craniectomies using polyethylene film have been performed on nineteen patients in the past twelve months. There have been no postoperative deaths, no wound infections, and no serious complications other than a severe laryngitis and tracheitis in one patient. The longest follow-up period for any patient is twelve months. Pericranium was not resected widely in that patient and film was placed only over one bone edge. There has been bony healing from the bone edge not covered with film but the craniectomies are still palpable. The patency of those craniectomies performed with wide removal of pericranium and wrapping of both bone edges

*Obtained from Harwid Plastics Company, 1108 Boylston St., Boston, Mass. Now available also in thinner sheets of 0.00226 cm.

with film has been much more satisfactory. The length of time since operation of most of the cases is insufficient to justify any final conclusions regarding the effectiveness of the polyethylene film in maintaining the patency of artificially created cranial sutures but the early results are most promising (Fig. 17).

SUMMARY AND CONCLUSIONS

1. Because of the rapid growth of the brain during the first year of life, it is to be expected that the best results from surgical treatment of premature closure of the cranial sutures will be obtained during this period. This has been confirmed in the series of cases described in this report. This fact places the responsibility for early suspicion and diagnosis of this condition upon the obstetrician and the pediatrician.

2. Of the fifty cases presented here from The Children's Hospital, forty-four patients have been treated by surgical procedures. (See Chart I and Tables I and II.) Twenty, or 40 per cent, were retarded to some extent before operation; 25 per cent of those treated surgically showed retardation after operation. Divided into separate groups, 24.4 per cent of the sagittal group, 37 per cent of the coronal group, and 83 per cent of those patients with two or more sutures fused showed mental retardation.

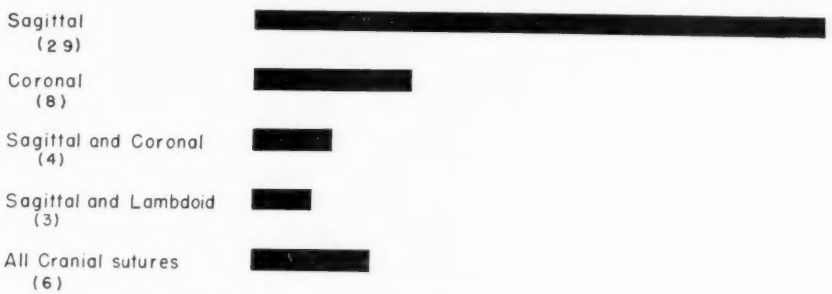


Chart I.—Craniosynostosis, sutures involved.

3. In the entire series, twenty patients received primary surgical treatment before the age of 1 year. Of this group there was only one definitely retarded patient.

4. Many patients, particularly those treated before 1940, came to the hospital at ages varying from 3 to 7 years. They were usually retarded when brought in for medical aid and little was to be expected from any surgical procedure. In spite of this, and often to the surprise of the physician, there was marked improvement in the patient's behavior at home.

5. Premature closure of the sagittal suture was the most common single type of synostosis found. It was involved in all the patients of the entire series except eight with premature closure of the coronal suture alone. Congenital anomalies are more frequently found in association with closure of the sagittal suture than in the normal population. No single anomaly has been found to predominate.

6. Premature closure of the coronal suture is usually associated with other congenital anomalies, particularly syndactylism of hands and feet.

TABLE I. AGE WHEN DEFORMITY WAS FIRST NOTED

AGE	NUMBER OF PATIENTS
At birth	32
1-3 months	6
3-6 months	2
6-9 months	4
9-12 months	1
Over 12 months	2
Unknown	3
Total	50

TABLE II. RELATION OF RESULTS TO INTERVAL BETWEEN ONSET AND OPERATION

	TOTAL	RETARDED
Less than 1 year	22	3
1-2 years	10	4
2-4 years	4	3
4-6 years	4	3
Over 6 years	4	3
Unoperated	6	4
Total	50	20

7. Patients observed over several years have been found to show gradual closure of other cranial sutures than those originally involved. It is, therefore, imperative to follow these patients with periodic physical examinations, mental evaluation, and roentgenograms.

8. The forty-four patients treated surgically have had a variety of decompressive operations, all of which have apparently been effective to some degree. Linear craniectomy with polyethylene film inserted over the bone edges to retard regeneration of bone has been adopted as the operation of choice. The present technique for this procedure has been described in detail.

9. In general the prognosis for mental development of a patient with premature closure of the cranial sutures treated under the age of 1 year is excellent, but if synostosis is evident at birth, surgical therapy should not be delayed more than a few weeks. It is inadvisable to delay operation until mental retardation becomes evident.

10. The mortality for operation on infants with craniosynostosis is negligible when proper supportive measures are provided.

REFERENCES

1. Sear, H. R.: Some Notes on Craniosynostosis, Brit. J. Radiol. **10**: 445-487, 1937.
2. Bolk, L.: Ueber prämature obliteration der nähte am menschenschädel, Ztschr. f. Morphol. u. Anthropol. **21**: 1-22, 1919.
3. Park, E. A., and Powers, G. F.: Acrocephaly and Scaphocephaly With Symmetrically Distributed Malformations of the Extremities. A Study of So-called "Acrocephalosyndactylism," Am. J. Dis. Child. **20**: 234-315, 1920.
4. Patterson, H. A.: Oxycephaly. An unpublished review of the cases of Dr. Harvey Cushing.
5. Greig, D.: Oxycephaly, Edinburgh M. J. **33**: 189-218, 280-376, 1926.
6. Scammon, R. S., and Dunn, H. L.: Empirical Formulae for the Postnatal Growth of the Human Brain and Its Major Divisions, Proc. Soc. Exper. Biol. & Med. **20**: 114-117, 1922.
7. Coppoletta, J. M., and Wolbach, S. B.: Body Length and Organ Weights of Infants and Children, Am. J. Path. **9**: 55-70, 1933.

8. Faber, H. K., and Towne, E. B.: Early Operation in Premature Cranial Synostosis for Prevention of Blindness and Other Sequelae, J. Pediat. **22**: 286-307, 1943.
9. Simmons, D. R., and Peyton, W. T.: Premature Closure of the Cranial Sutures, J. Pediat. **31**: 528-547, 1947.
10. Virchow, R.: Verhandl. d Phys.-med. Gesellsch. in Wurzb. **2**: 247, 1851, quoted from Faber, H. K.: Craniosynostosis (Oxycephaly and Related Disorders), Contributions to Medical Science, Ann Arbor, 1927, George Wahr, pp. 585-600.
11. Mount, L. A.: Premature Closure of Sutures of Cranial Vault. A Plea for Early Recognition and Early Operation, New York State J. Med. **47**: 270-276, 1947.
12. King, J. E. J.: Oxycephaly, Ann. Surg. **115**: 488-506, 1942.
13. Woodhall, B.: Oxycephaly; Results of Treatment by King "Morcellation" Method, J. Pediat. **20**: 585-595, 1942.
14. Lannelongue: De la craniotomie dans la microcephalie, Compt. rend. Acad. d. sc. **110**: 1382, 1890.
15. Lane, L. C.: Pioneer Craniectomy for Relief of Mental Imbecility Due to Premature Sutural Closure and Microcephalis, J. A. M. A. **18**: 49-50, 1892.
16. Ingraham, F. D., Matson, D. D., and Alexander, E.: Experimental Observations in the Treatment of Craniosynostosis, SURGERY **23**: 252-268, 1948.

THE ANTIBACTERIAL EFFECTS OF G-5,* G-11,† AND A-151,‡ WITH SPECIAL REFERENCE TO THEIR USE IN THE PRODUCTION OF A GERMICIDAL SOAP

PHILIP B. PRICE, M.D., AND ALBERTA BONNETT
SALT LAKE CITY, UTAH

(From the Department of Surgery, University of Utah School of Medicine)

EVER since the time of Robert Koch (1881) unsuccessful attempts have been made to produce a germicidal soap. The need for such a soap is obvious. The skin acts both as a barrier to microbic invasion of the body and as a carrier of potentially dangerous germs. Use of an effectively bactericidal soap would from both standpoints reduce the chances of infection.

Mechanical cleansing of skin with ordinary nonmedicated soap removes dirt, oils, and fats, as well as many loosely attached contaminating microorganisms, but the resident bacterial flora is not easily reduced.[1] Streptococci, pneumococci, diphtheria and influenza bacilli, and other susceptible pathogenic microorganisms are sometimes observed to have disappeared from hands after washing with ordinary soap, but staphylococci, colon bacilli, and sporulating anaerobes are more resistant. Yellow "kitchen soap" is more germicidal than bland white toilet soaps, as Kelly[2] demonstrated long ago, but that advantage is offset by its harsh irritating effect on skin. Pohle and Stuart[3] in 1941 reported that rosin soaps, or coconut oil soaps containing rosin, are more effective than ordinary soaps in degerming the skin.

Such studies are complicated by the tendency of many extraneous bacteria to disappear spontaneously from the cutaneous surface. This "self-disinfecting power" of skin remains poorly understood despite researches of Schiemann,[4] Arnold and associates,[5] Norton and Novy,[6] Burtenshaw,[7] and others.

It might appear easy at first thought to produce a germicidal soap simply by incorporating a germicide in soap. Many such preparations have been made, and some of them have been marketed with extravagant and unwarranted claims.

According to Gump,[8] a germicide added to soap should fulfill the following conditions: It should "retain its germ-killing powers in soap. It should not react with the soap constituents, or with the moisture contained in the soap. It also should not be influenced by the free alkali of the soap, nor by the alkalinity produced by the hydrolysis of the soap in the water. It should not be volatile and should not have a disagreeable odor. It should be relatively nontoxic, and should not be irritating to the skin or be a sensitizer. It should not stain the skin or cause spots on the laundry."

Very few chemicals meet these requirements. In fact, none of the familiar, time-honored germicidal soaps, tested by rigid standards, is found to have much disinfectant power.

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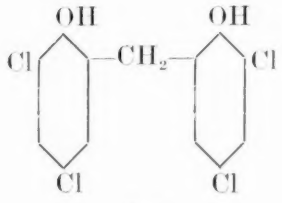
*G-5, bis-(3,5-dichloro-2-hydroxyphenyl) methane.

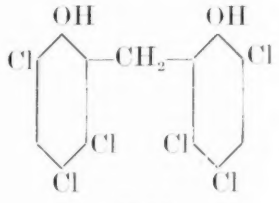
†G-11, bis-(3,5,6-trichloro-2-hydroxyphenyl) methane.

‡A-151, a complex salt of ethylene thiourea and silver nitrate.

Recently,* a number of hitherto untried chemical compounds were found to retain a large part of their bactericidal strength in the presence of excessive amounts of soap. Some of these compounds are di-phenols, derivatives of di-phenyl, dephenylsulfide, and diphenylmethane. Two of them, whose structures are indicated here, have for convenience been designated G-5 and G-11. Another promising substance, a complex salt of ethylene thiourea and silver nitrate, is called A-151.



G-5



G-11

A-151

G-5 and G-11 are white powdery compounds, virtually insoluble in water, but soluble in alcohol, acetone, and dilute alkali. A-151, a colorless crystalline compound, is soluble in hot water as well, but only sparingly in cold water. These three substances have been used in a new effort to produce a truly germicidal soap.

Of the three products, the one which has received most attention is G-11. Traub, Newhall, and Fuller[9] reported that 2 per cent G-11 soap used regularly for a week or more causes a pronounced reduction in the cutaneous bacterial flora. They claim that "a person using this soap regularly each time the hands are washed has a lower resident count after 2 minutes of washing than one who washes for 20 minutes with ordinary toilet soap." These conclusions were corroborated in general by Udinsky,[10] who employed simplified bacteriological tests, but extended his observations over a period of many months. More recently, Seastone[11] has reported similar results. We are informed[12] that G-11 soap in now being given a clinical trial in certain selected surgical clinics.

The present investigation was undertaken as part of a large scale critical study of skin disinfectants and skin disinfection.

PECULIAR ASPECTS OF THE PROBLEM

The insolubility of G-5, G-11, and A-151 in water makes it necessary to employ solvents—alcohol, acetone, or sodium hydroxide—which in themselves have antibacterial action. Attempts to elimate the bactericidal or bacteriostatic effect of the solvent by dilution with water results also in precipitation of indeterminable amounts of the chemical agent to be tested. For simple example, a 1:100 solution of A-151 in hot water is clear; diluted with 50 parts of cold distilled water, it turns cloudy; centrifuged rapidly for 1 hour, a clear supernatant fluid is obtained which retains a considerable amount of bacteriostatic activity.

*In the laboratories of the Givaudan-Delawanna Company.

It is believed by the manufacturers that the alkali of the soap in which G-5, G-11, and A-151 are incorporated serves to keep the chemicals in effective solution, but to what degree that is true in the presence of large amounts of water, especially hard water, or in culture media used for making bacterial counts, is unknown. That may be a consideration of some importance, since G-5 and G-11 inhibit bacterial growth when they are present even in minute amounts.

Another difficulty arises from lack of specific antidotes or neutralizing agents for phenolic compounds. It is conceivable that, as in the case of mercurial disinfectants, G-5, G-11, and A-151 unite in some way with bacterial cells, and that this union is not broken by subsequent dilution or washing with water. The chemical still attached to, or combined with, the cells may then inhibit their growth in cultures without killing them. A very common pitfall in all studies of disinfection lies in mistaking bacteriostasis for bactericidal effect. Unless a specific antidote is employed, which effectively removes or neutralizes the disinfectant being tested, gross misconceptions of its germicidal value may be obtained.

Seastone[11] has suggested the use of serum in media as an antidote for G-5 and G-11. Although serum probably does not neutralize these agents chemically, it does liberate some of the bacteria, as shown by significantly higher bacterial counts in serum agar plates. A-151, on the other hand, can be neutralized chemically without difficulty.

Another interesting complexity of these tests is that very minute quantities of G-5 and G-11 in cultures, amounts too small to have any bacteriostatic effect, seem to result in significantly higher counts than controls show. Whether that is due to breakup of coccal clumps, or to stimulation of certain bacteria which otherwise would not grow out, or to some other effect, we do not know.

IN VITRO TESTS

Scores of tests were made, using the three chemical agents in various concentrations against *Staphylococcus aureus*, *Staphylococcus albus* and *Escherichia coli*. A number of strains of *Staph. aureus* were utilized, one from a stock culture in our Bacteriological Laboratory, one (Strain 209) obtained from the U. S. Food and Drug Administration, Division of Bacteriology, Washington, D. C., and several isolated from the resident flora of our own hands. Results with these different strains were similar. Most of our tests consisted of culturing known numbers of vigorously growing test bacteria in poured agar plates. In germicidal tests, suspended organisms were exposed to graded concentrations of the disinfectant for measured lengths of time immediately before dilution and plating. In some of the tests for bacteriostasis, the chemicals were added to the bacterial suspensions before plating; in others, the chemicals were added to the agar before inoculation with test organisms. Accurate plate counts were made after forty-eight hours incubation in order to determine as nearly as possible the precise degree of killing or inhibition produced. The following is a highly summarized report of this work.

G-5 has powerful bacteriostatic action. A concentration of 1:4,000,000 in nutrient agar culture media causes complete or nearly complete inhibition of

TABLE I. BACTERIOSTATIC AND BACTERICIDAL EFFECTS OF G-5 AGAINST TEST BACTERIA IN VITRO

TEST	BACTERIA	DILUTION OF G-5	EFFECT
G-5 in agar media	*Staph. aureus*	1:4,000,000	Full inhibition
	Staph. aureus	1:10,000,000	No inhibition
	Esch. coli	1:50,000	Full inhibition
	Esch. coli	1:100,000	No inhibition
G-5 in soap in agar	Mixed skin flora	1:750,000	Marked inhibition
	Mixed skin flora	1:3,000,000	Almost no inhibition
G-5 in blood agar	*Staph. aureus*	1:1,000	Full inhibition
	Staph. aureus	1:10,000	No inhibition
Bacteria in suspension, exposed to G-5, then cultured	*Staph. aureus*	1:1,000	All killed after 30 seconds exposure
	Staph. aureus	1:100,000	None killed after 60 seconds exposure

Staph. aureus (Table I). Less than 1:10,000,000 has little or no bacteriostatic effect. That is true whether the original solvent is acetone or sodium hydroxide. Mixed skin organisms, mostly *Staph. albus*, appear to be slightly less susceptible to the bacteriostatic effect of G-5; *Esch. coli* is definitely more resistant.

The presence of blood or serum in media greatly reduces the bacteriostatic effect of G-5. A concentration of 1:1000 G-5 is required for complete inhibition of *Staph. aureus*, and there is no inhibition in strengths of 1:10,000 or less. (Seastone[11] noted similar effects with serum in his study of G-11.)

A solution of 1:1000 G-5 in weak acetone or sodium hydroxide solution appears to be capable of killing *Staph. aureus* suspended in water within 30 seconds at room temperature (about 25° C.). We have not been able to convince ourselves, however, that this is all bactericidal effect, and that bacteriostasis has no role in the production of negative cultures. Concentrations of G-5, 1:100,000 or weaker, appear to have no bactericidal effect on suspensions of *Staph. aureus* in 60 seconds at room temperature.

In dilutions as high as 1:5,000,000 or even 1:8,000,000 in agar media, G-11 causes complete or nearly complete inhibition of *Staph. aureus* (Table II). This bacteriostatic effect disappears when the dilutions are in the neighborhood of 1:20,000,000. *Esch. coli* grows with only slight reduction of counts in 1:1,000,000 G-11 media. These results parallel those of Seastone,[11] who in his qualitative tests used much heavier inocula than we have employed in our quantitative experiments.

1:1,000,000 G-11 in .01 N NaOH appears to kill suspensions of *Staph. aureus* after thirty minutes exposure at room temperature, but with exposures of only ten minutes normal counts are obtained. (Udinsky[10] reported that "1:1000

TABLE II. BACTERIOSTATIC AND BACTERICIDAL EFFECTS OF G-11 AGAINST TEST BACTERIA IN VITRO

TEST	BACTERIA	DILUTION OF G-11	EFFECT
G-11 in agar media	*Staph. aureus*	1:5,000,000	Full inhibition
	Staph. aureus	1:20,000,000	No inhibition
	Esch. coli	1:1,000,000	Slight inhibition
Bacteria in suspension, exposed to G-11, then cultured	*Staph. aureus*	1:1,000,000	All killed after 30 minutes exposure
	Staph. aureus	1:1,000,000	Very few killed after 10 minutes exposure

TABLE III. BACTERIOSTATIC AND BACTERICIDAL EFFECTS OF A-151 AGAINST TEST BACTERIA IN VITRO

TEST	BACTERIA	DILUTION OF A-151	EFFECT
A-151 in agar media	*Staph. aureus*	1:50,000	Full inhibition
	Staph. aureus	1:1,000,000	No inhibition
	Esch. coli	1:50,000	Full inhibition
		1:1,000,000	No inhibition
A-151 in soap in agar	*Staph. aureus*	1:50,000	Full inhibition
		1:100,000	No inhibition
Bacteria in suspension, exposed to A-151, then cultured	*Staph. aureus*	1:10,000	All killed after 60 seconds exposure
	Staph. aureus	1:500,000	None killed after 60 seconds exposure
	Esch. coli	1:10,000	None killed after 30 seconds exposure

G-11 will kill *Staphylococcus aureus* in five minutes at 37° C. when tested in accordance with the standard F. D. A. germicidal procedure.")

In contradistinction to G-5 and G-11, A-151 appears to be as effective against *Esch. coli* as against *Staph. aureus*. A-151 is bactericidal for *Staph. aureus* in concentrations of 1:10,000 or stronger with one minute exposure at room temperature, but 1:500,000 has no killing action (Table III). A quantity of 2 per cent A-151 soap sufficient to make a concentration of 1 part of the chemical in 50,000 parts of agar media causes complete inhibition of *Staph. aureus*, but a 1:100,000 concentration has no significant bacteriostatic effect. It has been noticed, however, that despite the availability of thioglycolate as an effective antidote, our tests with A-151 have given less consistent results than those with G-5 and G-11. The values in Table III are not to be considered exact, therefore, but rather as average findings in a large number of tests.

Obviously, all such in vitro tests have more academic interest than practical value. It is only when disinfectant agents are tested under conditions of actual use that their real merit can be determined.

SKIN DISINFECTION

These three compounds, G-5, G-11, and A-151, incorporated in soap, have been subjected to our serial basin test, [1, 13] which, though tedious to preform, provides more trustworthy information, we believe, than can be obtained in any other way. Advantages which may be claimed for the procedure are:

1. That it differentiates between transient and resident flora of the skin, and shows specific effects of germicides upon those two groups of microorganisms.

2. That it measures quantitatively and fairly accurately the size of the original bacterial population, the effect of any given disinfectant upon that population, and the size of the population left after the disinfectant is discontinued.

3. That it enables the disturbing factor of bacteriostasis to be avoided altogether, or at least to be detected and taken into account.

4. That it is designed specifically to test skin disinfectants under conditions of actual use.

5. That it facilitates qualitative studies of the cutaneous flora at various stages of washing or chemical disinfection.

6. That it permits subsequent observations on regeneration and restoration of the cutaneous bacterial flora.

The following soaps* were tested:

2 per cent G-5 in small cakes of relatively hard soap

6 per cent G-5 in small cakes of similar hard soap

2 per cent G-11 in larger cakes of high-grade softer soap

2 per cent A-151 in small cakes of hard brittle soap

Since these soaps were tested uniformly under conditions of ordinary use (by scrubbing with a brush in warm water), different amounts of soap came off on the brush and skin depending on the hardness of the soap used. Comparative weights of dried cakes before and after use showed that the amounts of soap actually used each minute of scrubbing averaged:

2 per cent G-5 soap, 0.473 Gm.

6 per cent G-5 soap, 0.590 Gm.

2 per cent G-11 soap, 1.020 Gm.

2 per cent A-151 soap, 0.303 Gm.

These measurements were taken into consideration in estimating the concentration of the chemical disinfectants in lather, wash water, and cultures.

Bacterial Effects of Scrubbing With the Disinfectant Soaps for Single Periods of One to Ten Minutes.—In these tests the hands and arms were first scrubbed with Ivory soap in a uniform manner in a series of basins of sterile water. One of the disinfectant soaps was then substituted for the Ivory soap

TABLE IV. DEGERMING EFFECT OF A THREE-MINUTE SCRUB WITH 2 PER CENT G-5 SOAP (ORIGINAL PRICE TEST); TIME SPENT IN EACH BASIN, 1 MINUTE

BASIN NUMBER	SOAP USED	BASIN COUNT	CUMULATIVE TOTALS	ACTUAL TOTALS
1	Ivory	825,000	2,143,000	3,893,000
2	Ivory	440,000	1,318,000	3,068,000
3	Ivory	240,000	968,000	2,718,000
4	Ivory	299,000	728,000	2,478,000
5	Ivory	256,000	429,000	2,179,000
6	Ivory	173,000	173,000	1,923,000
				1,750,000*
7	2% G-5	197,000	431,000	1,488,000
8	2% G-5	146,000	234,000	1,290,000
9	2% G-5	88,000	88,000	1,145,000
				1,057,000*
10	Ivory	139,000	607,000	1,057,000
11	Ivory	93,000	468,000	918,000
12	Ivory	48,000	375,000	825,000
13	Ivory	85,000	327,000	777,000
14	Ivory	80,000	242,000	692,000
15	Ivory	93,000	162,000	612,000
16	Ivory	69,000	69,000	519,000
				450,000*

*The number of bacteria left on the hands and arms after each series of washings.

*Prepared for us by the Givaudan-Delawanna Company.

in a second series of basins. Finally, in a third set of basins, scrubbing was resumed with Ivory soap. Cumulative totals of basin counts were plotted against time and the resultant curves were evaluated in relation to the washer's "standard" curve of bacterial population reduction by prolonged scrubbing with ordinary soap.

A typical test is shown in Table IV and Fig. 1. Concentration of G-5 in the lather in this instance was approximately 1:2000; in the washings (Basins 7 to 9), 1:430,000; and in the agar plate cultures, 1:4,700,000 or 1:9,000,000 depending on the size of sample plated. The lather containing G-5 was in contact with the skin for a total of about 135 seconds. All cultures of washings were made less than 5 minutes after the hands left the water. The concentration of G-5 in Basin 10 was estimated to be about 1:90,000,000 and in the subsequent washings G-5 was considered to be absent.

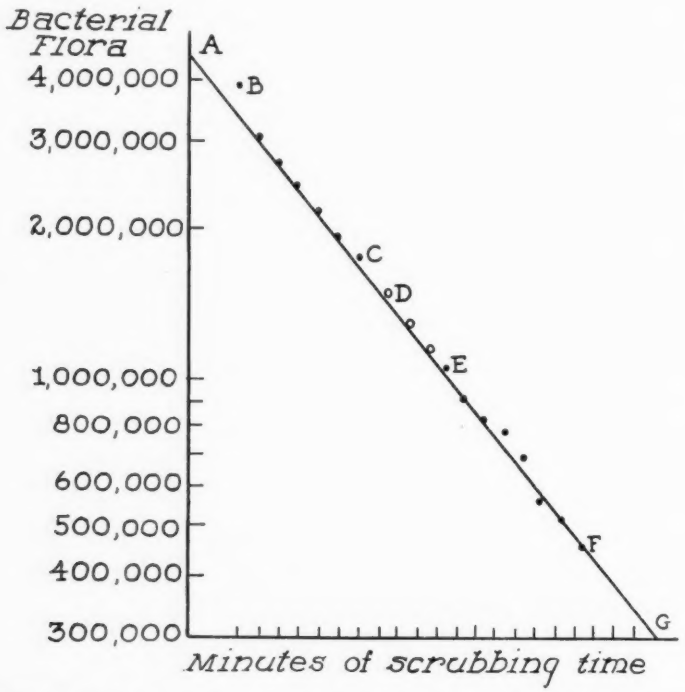


Fig. 1.—The actual totals (last column) of Table IV plotted against time to show graphically the bacteriologic effects of a single scrub of three minutes with 2 per cent G-5 soap. *AG*, the predetermined "standard" rate of bacteria removal by scrubbing with ordinary nonmedicated soap. *BC*, the effect of scrubbing with Ivory soap for six minutes. Deviation of the initial point is due to the presence of about 500,000 "transient" bacteria, all of which were washed off into the first basin. *DE*, the effect of scrubbing for three minutes with G-5 soap. *EF*, the effect produced when scrubbing is continued for another seven minutes with ordinary soap. Reduction of the flora from *C* to *D* (that is, from 1,750,000 to 1,488,000 bacteria) is attributed to the bactericidal and bacteriostatic action of G-5. This is a relatively small effect. Obviously almost the same result would have been obtained had Ivory soap been used throughout the experiment.

It is clear that in this test a three-minute scrub with 2 per cent G-5 soap reduced the bacterial flora of the hands and arms somewhat (from 1,750,000 to 1,057,000), but that this reduction is very little more than would have been accomplished by the use of ordinary soap for a similar period of time. Obviously,

TABLE V. EFFECTS OF FREQUENT WASHING WITH 2 PER CENT G-11 SOAP

SUBJECT	2 PER CENT G-11 SOAP USED FOR	HANDS LAST DISINFECTED (NO. OF DAYS AGO)	TOTAL BACTERIAL FLORA			RESIDENT BACTERIAL FLORA		
			EXPECTED	OBSERVED	REDUCTION* (%)	EXPECTED	OBSERVED	REDUCTION* (%)
A	16 hr. (3x)	7	8,500,000	2,600,000	31.0	7,800,000	1,100,000	14.0
B	18 hr. (7x)	7	18,000,000	4,460,000	25.0	16,000,000	4,460,000	26.0
A	2 days	7	8,500,000	1,780,000	21.0	7,800,000	1,100,000	13.0
B	2 days	7	18,000,000	2,200,000	12.2	16,000,000	1,800,000	11.2
B	4 days	7	18,000,000	580,000	3.2	16,000,000	580,000	3.6
A	7 days	5	4,700,000	240,000	5.1	4,000,000	200,000	5.0
B	11 days	7	18,000,000	620,000	3.4	16,000,000	620,000	3.8
A	16 days	11	8,500,000	470,000	5.5	7,800,000	360,000	4.6

EFFECTS OF DISCONTINUING THE USE OF 2 PER CENT G-11 SOAP

SUBJECT	2 PER CENT G-11 SOAP DISCONTINUED FOR	HANDS LAST DISINFECTED (NO. OF DAYS AGO)	TOTAL BACTERIAL FLORA			RESIDENT BACTERIAL FLORA		
			EXPECTED	OBSERVED	CHANGED* (%)	EXPECTED	OBSERVED	CHANGED* (%)
B	7 days	7	18,000,000	17,900,000	100.0	16,000,000	15,000,000	93.0
A	14 days	14	8,500,000	19,200,000	210.0	7,800,000	12,400,000	148.0

*Observed flora divided by expected flora.

most of the bacteria removed while scrubbing with the G-5 soap were recoverable in viable form in the washings of Basins 7 to 9. Whether the 262,000 bacteria not accounted for (the absolute total after Basin 6 minus the absolute total of Basin 7) were killed by the chemical during the three-minute lather period, were inhibited in culture media, or represent technical error, we do not know.

A comparison of these results with the in vitro findings of Table I is instructive.

From many such tests we have drawn the following general conclusions:

1. None of the disinfectant soaps under investigation is much superior to ordinary nonmedicated soap when used for single brief periods of washing or scrubbing.

2. Of the four preparations tested, 6 per cent G-5 soap was the most effective, and 2 per cent A-151 least effective, but only by narrow margins.

3. The G-5 soap preparations were slightly irritating to skin, however, whereas G-11 and A-151 soaps were quite innocuous.

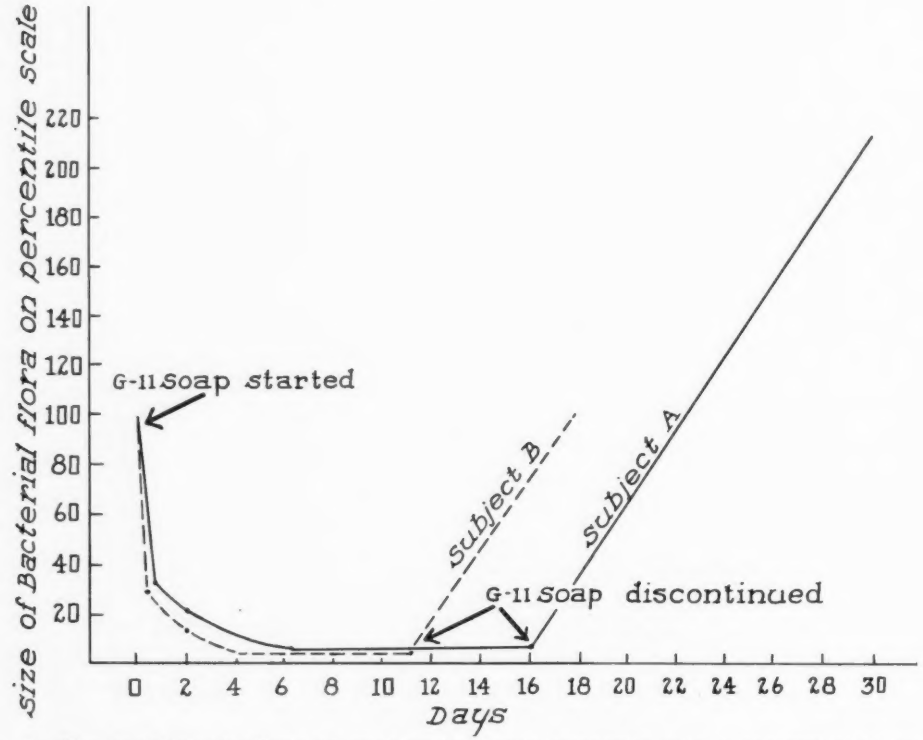


Fig. 2.—The bacteriologic effects of washing the hands frequently with 2 per cent G-11 soap; restoration of the cutaneous bacterial flora after disuse of the disinfectant soap.

Bacterial Effects of Repeated, Frequent Washing With 2 Per Cent G-11 Soap.—Table V and Fig. 2 summarize the results of a number of tests made on subjects A and B. These two individuals prior to the tests had for various periods of time used G-11 soap every time they washed or bathed. Other disinfectant agents, such as alcohol, had not been used for several days, prior to each test, as shown in Column 3. What their bacterial counts would have been

had the disinfectant soap not been used must be estimated by averaging a large number of preliminary control tests; consequently, the "expected" values listed in the table are only approximations. By the same token, the effects of frequent washing with G-11 soap, expressed in terms of percentage reduction of the usual flora, are no more than approximations.

In general the tests seem to show that the bacterial flora of skin is reduced by frequent repeated washing with 2 per cent G-11 soap, maximal reduction being reached after four to seven days of use. Continued use of the soap does not reduce the bacterial population further, but does keep it at a low level of about 5 per cent of the usual number.

When use of G-11 soap is discontinued, the cutaneous flora regenerates promptly and returns to normal proportions in approximately seven days. A similar regeneration rate occurs after disinfection of the skin by other means,[1] which suggests that G-11 soap has little if any lasting effect in keeping the cutaneous flora low once its use is discontinued.

Additional tests were made with five members of our operating room staff, three surgical residents and two nurses. Since these individuals did not have "standard" curves established, the absolute effects of G-11 soap on their cutaneous microbic populations were not determined. Bacterial counts of serial basin washings indicated, however, that the usual flora of the hands and arms of these persons were markedly reduced by daily frequent washing with 2 per cent G-11 soap for one week, but that failure to use the soap constantly resulted in prompt return to higher counts. Many transient bacteria were found on all the hands, even when the disinfectant soap was being used regularly. The impression was gained that the soap was more effective in keeping the resident flora low than in preventing the skin from picking up contaminants.

It was estimated that in using 2 per cent G-11 bar soap for scrubbing, the concentration of the chemical in lather was about 1:600, and that a similar concentration could be obtained by employing a liquid soap containing 0.2 per cent G-11. Accordingly, this latter preparation was placed in soap dispensers in the operating room, where for six months it was used unwittingly by a large number of persons in routine preoperative scrubs. No ill effects upon the skin were noticed. On the other hand, tests made on representative individuals showed that their cutaneous bacterial flora was on the average no lower than when ordinary nonmedicated liquid soap was employed. In order to keep the bacterial flora significantly reduced, it was necessary for these individuals to keep cakes of G-11 soap in their rooms and on the wards where they could be used many times daily.

Thorough qualitative studies were not made of organisms found in washings before and after use of G-11 soap, but differential counts made in representative experiments showed that the proportionate number of yellow pigment-producing surface colonies was not significantly altered by the use of G-11 soap.

MISCELLANEOUS OBSERVATIONS

A number of patients facing elective "clean" operations were given cakes of 2 per cent G-11 soap with instructions to bathe the site of operation several

times daily for four or more days prior to surgery. At the time of operation the skin was disinfected in the customary manner with alcohol, ether, and a mercurial or iodine. None of these patients showed any infection or inflammation in the wounds. Equally good results were obtained, however, in a parallel group of cases in which G-11 was not used. Obviously a clinical test of this sort is without significance. The incidence of postoperative infection in any group of patients is the net result of so many variable factors, difficult or impossible to control, that it cannot be relied upon to measure the influence of any one variable—in this instance the use or nonuse of G-11 soap.

Fresh scratches and abrasions of the skin washed with G-11 soap smarted slightly and became mildly inflammed, but no more perhaps than when any other soap of equal alkalinity was employed.

One individual with acne of the face has been kept under observation for more than eighteen months during which time 2 per cent G-11 soap has been used intermittently. Although the soap has not cured the acne, its repeated daily use for extended periods of time definitely reduced the incidence of pustules, and each time the soap was discontinued, the number of infections increased.

G-11 is reported by Gump[8] to be relatively nontoxic when given orally to guinea pigs. Injected intravenously, however, in 0.01 N NaOH solution G-5, G-11, and A-151 were found by us to be highly toxic. As little as 35 mg. in dogs weighing 7 or 8 kilograms usually caused death within a few minutes, characterized by convulsive movements, sudden respiratory cessation, and widespread intravascular clotting of blood. The remaining fluid blood had negligible bacteriostatic power. The 0.01 N NaOH solution alone had no such effect.

COMMENT

Washing or scrubbing leaves on the skin a film of soap[14] which is not entirely removed by ordinary rinsing. A thin layer of G-11 probably persists on the hands for some time after each washing, and is responsible for the slow but pronounced reduction of the resident bacterial flora which occurs whenever the disinfectant soap is used many times daily for several days. If that assumption is correct, any washing without G-11 soap would be disadvantageous in that the G-11 on the skin might thus be washed away permitting regeneration of the bacterial flora.

There can be little doubt that G-11 soap has real merit, and that used properly it can contribute materially to the perfection of aseptic surgical technique. Patients preparing for elective surgery would do well to bathe the field of operation with the soap frequently (five or six times a day) for four or more days preoperatively. Such a routine would be far more effective bacteriologically and less harmful psychologically than the old-fashioned "evening ward prep" of skin painting and sterile dressings still in vogue in some quarters. Dentists, whose hands pass from one highly contaminated mouth to another, would be well advised to wash with G-11 soap between each case. Physicians and surgeons would probably find it advantageous to use the soap regularly in their offices and homes. Hospitals might even consider using no other soap

than G-11 throughout the entire institution. Under such conditions it might be expected that nurses, interns, residents, maids, orderlies, and cooks would all carry fewer bacteria on their hands than they do using ordinary soap.

A word of caution should be added, however. G-11 soap has its limitations. It would be unfortunate indeed if those who use the soap permit their enthusiasm to engender a false sense of security against infection. Since effective reduction of the resident bacterial population of skin depends so largely on the frequent and unremitting use of G-11 soap, and since a potentially dangerous transient flora may at any time be present on the hands, it would seem unwise to discard other chemical germicides and depend entirely upon G-11 soap for skin disinfection. We strongly recommend, for the present at least, that the customary preoperative scrub and hand disinfection routine be carried out in full even though G-11 soap has been used. Likewise the field of operation should be treated as heretofore with germicidal solutions immediately before draping. Disinfection of the skin is difficult and uncertain at best. The present well-established methods of skin disinfection may be supplemented to advantage, but probably should not be supplanted, by the use of G-11 soap.

It has been suggested that traces of G-11 on skin simply inhibits proliferation of the resident flora, and that this action may protect the operative wound from a torn glove. Unfortunately, there is little evidence to support such a contention. The action of G-11 on skin is clearly bactericidal as well as bacteriostatic. Surviving microorganisms which come off hands which have been washed with G-11 soap grow without inhibition in ordinary culture media (see Table IV and Fig. 1). It would not, therefore, be safe to assume that similar organisms escaping through a torn glove are unable to live and multiply in a wound.

SUMMARY AND CONCLUSIONS

Three new chemical compounds, for convenience designated G-5, G-11, and A-151, have been used in a fresh attempt to produce a truly germicidal soap.

Investigation of the antibacterial power of these compounds is frought with unusual difficulties because of their insolubility in water, the bacteriostatic effects of even minute traces of the substances in culture media, and lack of effective neutralizing agents for G-5 and G-11.

In vitro tests show that all three compounds, and G-11 in particular, are powerfully bacteriostatic, but their germicidal activity is less impressive.

The three compounds incorporated in soap have been tested under conditions of actual use by means of our serial basin method. This test, in our opinion, gives more information and more reliable results than any of the simplifications of the test which have been employed by other investigators.

Single periods of scrubbing for one to ten minutes with these disinfectant soaps do not reduce the bacterial flora of the hands and arms more rapidly than similar scrubs with ordinary nonmedicated soap.

Two per cent G-11 bar soap used many times daily for four or more days reduces the resident bacterial flora of skin to about 5 per cent of its ordinary size. Continued use of the soap several times every day appears to keep the

flora at that low level. If the soap is used only for preoperative scrubbing, but not between times, a persistently low flora is not maintained.

Washing with G-11 soap does not protect the skin from subsequent contamination with extraneous bacteria. Even when the disinfectant soap is being used regularly, a relatively large transient flora may be found on the hands between washings; and whenever use of G-11 soap is discontinued, regeneration of the cutaneous flora proceeds at the same rate as though the hands had been disinfected by other means.

G-11 soap does not appear to have a selective action against pathogenic bacteria on the skin. There is reason to believe that the numerical ratio between pathogenic and nonpathogenic microorganisms is approximately the same before and after disinfection with G-11 soap.

The antibacterial activity of G-5, G-11, and A-151 is greatly reduced in the presence of blood or serum. Injected intravenously, these compounds are highly toxic. They probably should not be used in wounds.

Of the preparations tested, 2 per cent G-11 bar soap appears to offer most from a practical standpoint. Used rationally and faithfully, G-11 soap is probably capable of contributing materially to the perfection of aseptic surgical technique, but in our judgment it should not be employed to the exclusion of the present routine postoperative scrub or the customary chemical disinfection of hands and fields of operation.

REFERENCES

1. Price, P. B.: Bacteriology of Normal Skin; New Quantitative Test Applied to Study of Bacterial Flora and Disinfectant Action of Mechanical Cleansing, J. Infect. Dis. **63**: 301, 1938.
2. Kelly, H. A.: Hand Disinfection, Am. J. Obst. **24**: 1414, 1891.
3. Pohle, W. D., and Stuart, L. S.: The Germicidal Activity of Rosin Soap and Fatty Acid Soap as Indicated by Handwashing Experiments, Oil & Soap **18**: 1, 1941.
4. Schiemann, O.: Ueber Handedesinfekton und Handereinigung in Ihrer Bedeutung zur Verhütung von Krankheitsübertragungen, Ztschr. f. Hyg. u. Infektionskr., Leipzig **88**: 129, 1919.
5. Arnold, L., and others: Self-disinfecting Power of Skin as a Defense Against Microbic Invasion, Am. J. Hyg. **11**: 345, 1930.
6. Norton, J. F., and Novy, M. F.: Studies on Self-disinfecting Power of Skin, Am. J. Pub. Health **21**: 1117, 1931.
7. Burtenshaw, J. M. L.: Mortality of Haemolytic Streptococcus on Skin and on Other Surfaces, J. Hyg. **38**: 575, 1938.
   Idem: Mechanism of Self-disinfection of Human Skin and Its Appendages, J. Hyg. **42**: 184, 1942.
8. Gump, W.: The Development of a Germicidal Soap, Soap & Sanitary Chemicals & The Givaudan, March and April, 1945.
9. Traub, E. F., Newhall, C. A., and Fuller, J. R.: Value of New Compound Used in Soap to Reduce Bacterial Flora of Human Skin, Surg., Gynec. & Obst., **79**: 205, 1944.
   Idem: New Cutaneous Bactericidal Agent Used in Soap, Arch. Dermat. & Syph. **52**: 385, 1945.
10. Udinsky, H. J.: Reduction in Total Skin Flora by Daily Use of Soap Containing Dihydroxyhexachlorodiphenylmethane, J. M. Soc. New Jersey **42**: 15. 1945.
11. Seastone, C. V.: Observations on the Use of G-11 in the Surgical Scrub, Surg., Gynec. & Obst. **84**: 355, 1947.
12. Gump, W.: Personal Communication.
13. Price, P. B.: New Studies in Surgical Bacteriology and Surgical Technic, With Special Reference to Disinfection of Skin, J. A. M. A. **111**: 1993, 1938.
   Idem: Ethyl Alcohol as a Germicide, Arch. Surg. **38**: 528, 1939.
14. Miller, B. F., Abrams, R., Huber, D. A., and Klein, M.: Formation of Invisible, Nonperceptible Films on Hands of Cationic Soaps, Proc. Soc. Exper. Biol. & Med. **54**: 254, 1943.

Surgical Technique

TECHNIQUE OF INGUINAL NODE DISSECTION

IVAN D. BARONOFSKY, M.D., MINNEAPOLIS, MINN.

(From the Department of Surgery, University of Minnesota Medical School)

INGUINAL NODE DISSECTIONS

During the past few years there has been considerable interest in this clinic in the technique and indications for inguinal node dissection. It is common knowledge that such wounds frequently heal very slowly and rarely by primary intention.

ANATOMY OF THE INGUINAL AREA

Common usage of the term inguinal dissection has been interpreted as not only that area of the abdominal wall which is nearest the thigh, but also that area of the thigh which includes the femoral triangle. In our discussion the term inguinal will be interpreted as such.

Blood Supply of Skin of Inguinal Area.—The skin over the inguinal area is supplied by the superficial external pudendal artery, the superficial circumflex iliac artery, and the superficial epigastric artery. These in turn anastomose with the cutaneous branches of the inferior epigastric artery. The main branches of these arteries run in a fashion which parallels the inguinal ligament and the skin creases of the lower abdomen and upper thigh. As will be described later, during the dissection of the skin flaps, these vessels' tributaries can be seen very clearly just within the fatty layer of the superficial fascia of the skin (Camper's fascia). The direction of the vessels is parallel to the inguinal ligament.

The Femoral Triangle.—The femoral trigone is a triangular space lying immediately distal to the inguinal ligament. This ligament forms the base of the triangle. The oblique lateral boundary is the medial margin of the sartorius muscle and the medial border of the adductor longus muscle. The roof consists of the fascia lata which completely covers the space anteriorly. The floor is made up of two inclined planes, which form a well-marked median groove at their junction. The lateral inclined plane consists of the iliopsoas muscle invested by a thin layer of fascia. The adductor magnus and pectineus muscles, both of which are invested with fascia lata, form the median plane. The most important contents of the triangular space, included between the fascial roof and floor of the femoral triangle, are the femoral vessels and nerve and their branches. These structures, the termination of the great saphenous vein, the deep subinguinal lymph vessels and glands are embedded in a quantity of loose fatty tissue.

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Lymph Nodes.—The inguinal nodes, as we employ the term, refers to all lymph nodes in the inguinofemoral region. The glands are arranged as a superficial and a deep group.

The superficial group is arranged as: (a) a proximal group parallel to the inguinal ligament (superficial inguinal glands); (b) a distal chain on the sides of the long saphenous vein (superficial subinguinal glands).

The chief efferent lymph vessels from the superficial nodes extend either directly into the external iliac lymph nodes above the inguinal ligament or to the deeper inguinal nodes beneath the fascia. These deep lymph nodes are situated laterally and medially to the femoral vein. The highest and most constant of these deep nodes in the femoral triangle is the so-called Cloquet's or Rosenmüller's node, situated on the medial aspect of the femoral vein at the entrance to the femoral canal, or actually within it.

Both the superficial and deep inguinal nodes drain into the external iliac chain, a group of nodes of the periaortic chain. Young called attention to a small node located at the external inguinal ring.

REGIONAL LYMPHATIC DRAINAGE

As a rule the lower trunk area drains toward the groin. The upper trunk area drains toward the axillary vessels. The dividing line is usually extended to between the umbilicus and the small of the back.

The lower extremities drain entirely into the inguinal glands. Rarely, deeper structures around the gluteal region may drain to hypogastric nodes via lymphatics accompanying the gluteal vessels.

There is a very free anastomoses of lymphatic vessels draining the external genitals, and thus bilateral or crossed metastasis is common. In the main, the lymphatic drainage from the external genitals reaches the superficial femoral nodes, chiefly of the superficial external pudendal group. From the glans penis and clitoris, deeper lymphatic vessels may pass directly to the deep femoral nodes, or by way of the inguinal canal to the external iliac nodes.

The lymph drainage of the scrotum is remarkably abundant. The collecting lymph vessels originate along the median raphe and anastomose freely with those of the opposite side. On this account the metastases are nearly always bilateral, and accordingly bilateral groin dissections are indicated.

The lymphatic drainage of the vulva is very extensive also. Malignancies of this area should eventually, therefore, have bilateral dissections.

The lymph drainage of the perianal and perienal regions is to the superficial inguinal glands. The extensive intercommunication of both sides of this area is such that bilateral dissection must also be done.

It may be well to insert a word here on the lymphatic drainage of the rectum, anus, and vagina. The classic description of the lymphatic spread of carcinoma of the rectum has been written by Miles (1931). McVay (1922), Gilchrist and David (1938), and Coller, Kay, and MacIntyre (1940) have contributed much to the surgeon's knowledge of lymphatic spread of low-lying carcinomas.

The lymphatics of the rectum may be classified as the extramural and intramural groups. The intramural lymphatics consist of two freely communicating networks located within the wall: one, the submucosal and the other, the intermuscular network. These intercommunicate by radial lymph channels lying between the circular muscle fibers. The submucosal network is to a lesser extent continuous above, with the pelvic colon, and below, with the subcutaneous lymph channels of the anus and perianal skin. The intermuscular network lying between the circular and longitudinal muscle coats communicates with similar channels of the pelvic colon above, and with those of the external sphincter below.

These intramuscular lymphatics in turn drain into the intermediary system which is located between the external muscular coat and the perirectal fat. This system drains into the lymphatics accompanying the superior, middle, and inferior hemorrhoidal arteries, which is the extramural lymphatic system. Thus, spread of a carcinoma of the rectum may occur superiorly, laterally, or inferiorly.

The lymphatics of the anus drain mainly into the superficial nodes of the groin. However, it is well to remember that tumor emboli may spread upward into the rectal lymphatics by means of the communications described previously, as well as the reverse occurring.

The lymphatic pathways of the vagina have abundant connections with the anal region and the vulva. The usual spread of carcinoma is one that will lead into the iliac and hypogastric nodes. But that there is a connection of lymphatics via the vulva into the inguinal area must be noted. The frequent involvement of inguinal area in lymphogranuloma inguinale adds proof to its presence.

INDICATIONS FOR GROIN DISSECTIONS

Groin dissection is indicated in metastatic cancers occurring in the inferior extremity, male and female genitals, the perineum, the perianal zone, gluteal region, and the infraumbilical segment of the abdominal wall. There is some question as to whether one should wait for definite evidence such as clinically palpable nodes in cases of epidermoid carcinoma of the extremities. Pack and Rekers (1942) stated that 24 per cent of patients with controlled epidermoid carcinomas of the hands and feet, and without palpable regional lymph nodes, subsequently developed nodal metastases while under observation. They suggested that if dissection of these regional lymph nodes had been routinely done on admission, 75 per cent of them would have been unnecessary. However, I believe that even 75 per cent of unnecessary operations in the treatment of an otherwise lethal disease is a small risk.

Dean (1935) stated the experience of the Memorial Hospital in examination of inguinal nodes in epithelioma of the penis. An error of 14 per cent is made in determining the presence or absence of metastases in inguinal nodes as diagnosed by physical examination alone. At the time of the first examination, inguinal adenopathy is present in about 76 per cent of the patients. Approximately one-half of the nodes were cancerous as proved by biopsy later.

Colby and Smith pointed out the inadequacy of physical examination alone. In a series of thirty-two cases of groin dissection for carcinoma of the penis, eleven of the total were dissected although no nodes were palpable. In four, or 36.3 per cent, malignant glands were found on microscopic examination.

Groin dissection may be justified as a palliative procedure, even when involvement is extensive with beginning necrosis, provided that the disease can be freed from the great vessels. Any procedure which may prevent the necrotic discharging ulcerations in the groin with the attendant infections and hemorrhages constitutes excellent palliation.

The presence of intercommunicating systems of lymphatics between the lower rectum, anus, and vagina, raises a question: Should inguinal node dissection be considered in lesions of the lower rectum and vagina? Gilchrist and David (1948) have shown that 4.6 per cent of tumors of the rectum below the promontory may have retrograde metastases. They have also shown that when a lymph node is destroyed or blocked, the lymph drainage is rerouted through collateral channels or by retrograde means, into a channel draining into a normal node.

At the University of Minnesota Clinic, a careful examination of the inguinal area is made both preoperatively and in the follow-up period in those patients who have had surgery for low rectal lesions. We have come to believe that anal lesions routinely should have an abdominoperineal resection followed by bilateral inguinal node dissections.

Pack and Rekers (1942) enumerated the following postulates for successful groin dissection:

(1) The primary cancer, wherever located, should be controlled or controllable and should be treated first.
(2) There should be no clinical evidence of blood stream metastases.
(3) The lymph stream must be centralward without evidences of blockage and retrograde extension.
(4) It should be technically possible to excise all of the lymph nodes involved as suspected of becoming involved.
(5) There must be some possibility of interruption of the lymphatic spread of the cancer by an excision of these nodes.
(6) There should be evidence that the cancer has drained only to the regional groups of nodes to be attacked in the groin dissection.

TIME OF DISSECTION

Some surgeons have devised en bloc procedures combining groin dissection with operations on the primary focus of disease. (Basset in 1912, Taussig in 1935, and Young in 1931.) In general, however, dissection of the inguinal group of nodes when indicated is carried out as a later procedure two to three weeks after complete control of the primary disease. The groin dissection should not be postponed too long if metastases are clinically evident.

SKIN NECROSIS FOLLOWING DISSECTION

Skin necrosis is a postoperative complication following dissection has been one of the most distressing and frequent causes of morbidity. Taussig (1935) in

a review of thirty-eight Basset operations stated: "In spite of many cases of infected wounds, there were no deaths from sepsis." Lewis (1931), in reviewing the results of Young's radical operation for carcinoma of the penis, presented nineteen cases of infection with slough out of a total of thirty-four dissections. Pack and Rekers had an incidence of 26 per cent of badly infected wounds out of a total of 122 groin wounds. Taylor and Nathanson (1942) in their monograph on lymph nodes did not give figures as to wound infection but implied that it occurs with distressing frequency. McKelvey (1947) has suggested that the less undermined skin left in dissection for vulvar carcinoma, the better the primary healing. He practices the wider excision of skin over the inguinal area with primary closure.

The causes of necrosis of the skin have been attributed to various feators: (1) the presence of a large dead space over the femoral triangle following removal of the lymph nodes, fascia, and fat; (2) the thin skin flaps; (3) inadequate pressure dressings; (4) the presence of bacteria with lymph nodes from the anus and perineal regions which drain into the inguinal area.

Though these may be factors that are important, it is our impression that careful attention to the fundamental principles of surgical wound healing will obviate this distressing complication. Though it is to be admitted that chemotherapy has aided us materially in cutting down the postoperative morbidity of many surgical procedures, it cannot correct any errors of fundamentals and principles.

TECHNIQUE OF GROIN DISSECTION

The patient is placed on the operating table with the corresponding thigh slightly abducted and externally rotated. Any satisfactory anesthetic agent may be used; however, if bilateral dissection is to be carried out, general anesthesia is used.

The skin incision differs from that suggested by Basset and Taussig. They have suggested a vertical incision. I believe that this type of incision is the cause of the high incidence of wound infection. As was pointed out in the discussion on the blood supply of the skin of the inguinal region, these vessels run in the superficial fascia in a manner parallel to the inguinal ligament. A vertical incision would cut across the blood supply to the medial flap. Our incision, therefore, is about a 14 cm. incision parallel to and about 5 cm. below the inguinal ligament. In its course, the middle of the incision is over the palpable femoral artery. Unless the skin is involved, no skin is removed with the specimen.

The incision is then carried down to Camper's fascia, which can be identified as a definite layer by careful traction upward with a fine rake retractor. The small blood vessels can be seen coursing in the fat immediately above. Skin towels when applied should be clipped with the lightest towel clips possible as heavy manipulation will thrombose the fine vessels to the edges and necrosis will result.

The dissection of the upper flap is then carried out by means of sharp dissection, along Camper's fascia, until a point 2 inches above the inguinal liga-

ment is reached (Fig. 1). The dissection then has exposed the anterior superior spine and the external abdominal ring. The scalpel is then turned downward and the fat and fascia over the external oblique aponeurosis are cleaned meticulously down to the inguinal ligament. At this point the lower skin flap is dissected down to the apex of the femoral triangle. The long saphenous vein is encountered and divided, when the dissection at this point is carried down and through the fascia lata overlying the muscles in this area. The finest 00000 silk (Deknatel) is used throughout except for the larger veins or arteries encountered, for which 0000 silk is used.

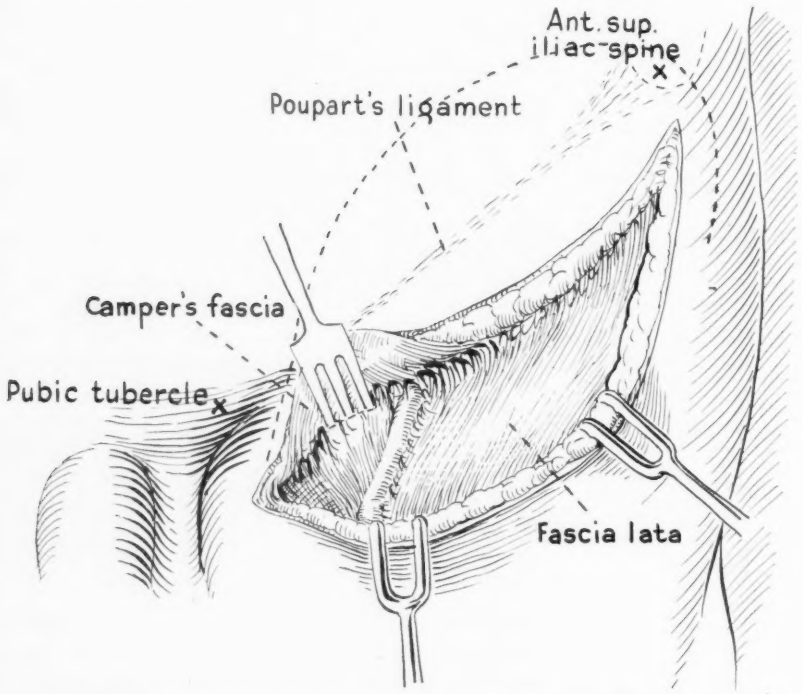

Fig. 1.—Illustration showing the incision and early dissection of upper flap. The curved broken line gives the limit of dissection of this flap. It extends to a point two inches above the inguinal ligament.

Having outlined both skin flaps, the fascia lata is then incised at the lateral border of the sartorius and the medial border of the adductor longus (Fig. 2). The dissection is then carried out carefully in a centripetal manner from below upward and from either side inward so that at the end of the procedure the specimen will be attached only by means of the saphenous vein entering the femoral vein (Fig. 3).

In dissecting out the femoral vessels, the adventitial layer of the artery and vein is stripped together with the fat and fascia intervening between these vessels. Near the lower angle of the femoral triangle several small lymphatics may be encountered which should be ligated.

The dissection then is carried from above downward crossing the inguinal ligament toward the saphenous vein. The femoral vessels are again stripped

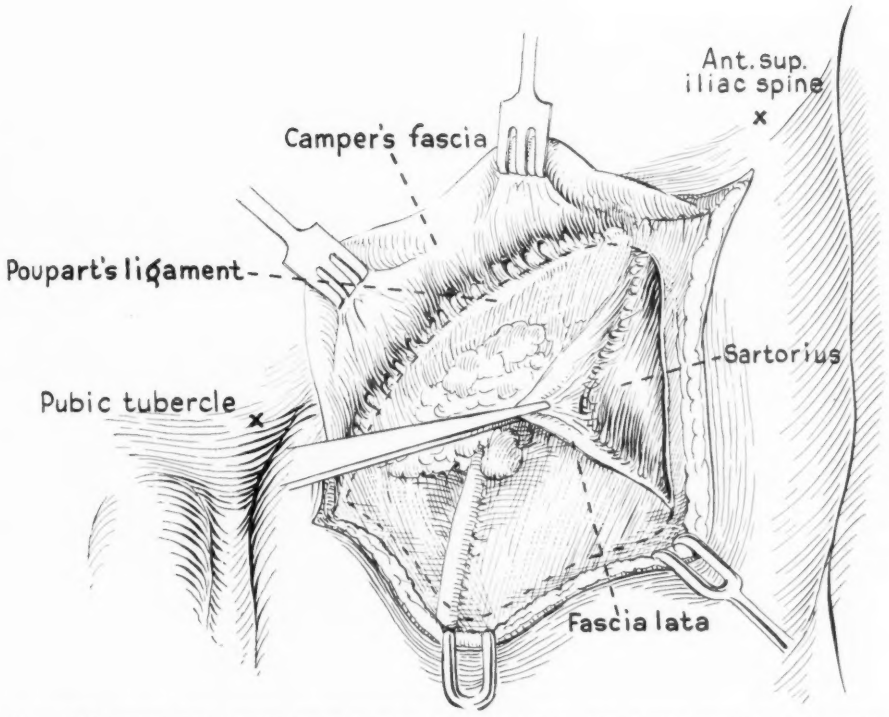

Fig. 2.—Both upper and lower flaps having been outlined, the fascia lata is then incised at the lateral border of the sartorius and the medial border of the adductor longus.

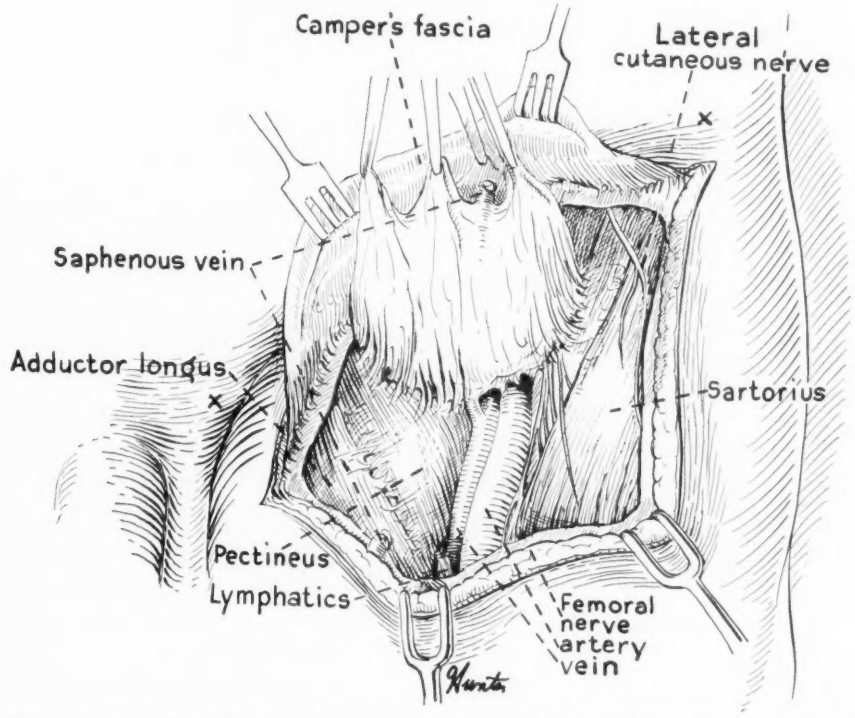

Fig. 3.—The dissection is then carried out carefully in a centripetal manner from below upward and from either side inward, so that at the end of the procedure the specimen will be attached only by means of the saphenous vein entering the femoral vein.

carefully of adventitia, fat, and fascia. Along the medial side of the femoral vein, the femoral canal is carefully cleaned. The inguinal ligament is retracted upward and the vessels cleaned as far as possible. The spermatic cord should be palpated during the dissection and the fascia overlying it dissected with the specimen.

During the dissection care must be taken to preserve the various cutaneous nerves to the thigh if they are not involved, as an annoying anesthesia will result.

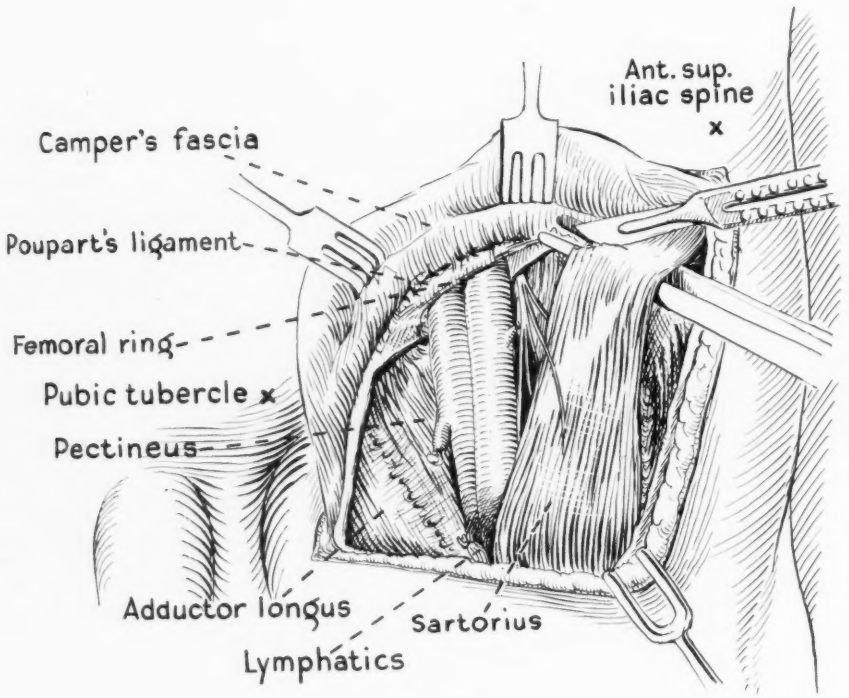

Fig. 4.—Sartorius muscle being cut at its origin at the antero superior spine.

Having completely and carefully bared the femoral triangle, the saphenous vein is then ligated and cut and the block specimen removed. A triangular defect is thus left around the femoral vessels. This is filled in by means of the following maneuver, a procedure first carried out in this clinic by Owen H. Wangensteen: The sartorius muscle is cut at its origin at the anterosuperior spine (Fig. 4). It is then swung over the defect present about the femoral vessels; this transplantation of the sartorius muscle suffices to cover the femoral vessels nicely. Fine 0000 silk sutures are then placed between the upper cut end of the muscle and the inguinal ligament above the femoral vessels. Especial care must be observed in suturing the muscle above the femoral canal to prevent a hernia from occurring. Suture of Cooper's ligament to Poupart's ligament is often carried out as a prophylactic measure.

The lateral side of the muscle is then sutured to the iliacus with a series of interrupted sutures. This is repeated on the medial side approximating the sartorius to the adductor longus (Fig. 5).

Hemostasis being complete, the final stage of the dissection is begun. Fine 00000 silk sutures approximate the undersurface of the skin flaps to the sartorius muscle. These are staggered and are put in so that there is a minimal dead space between the flaps and the underlying muscle. This will also relieve any tension on the skin approximation if some has been removed because of involvement.

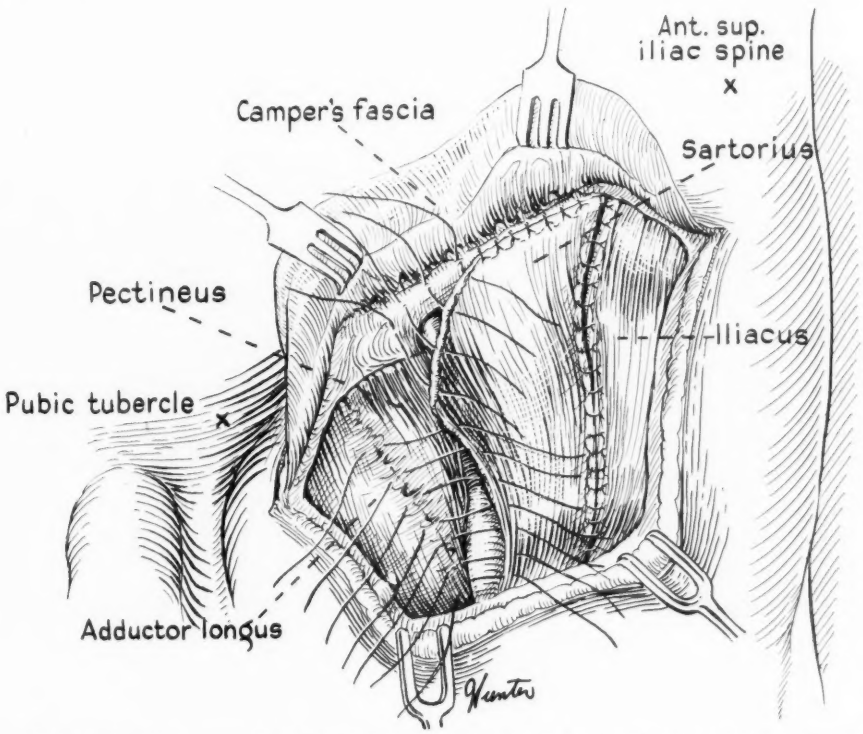

Fig. 5.—Sartorius muscle has been swung over the defect present about the femoral vessels. Fine 0000 Deknatel silk sutures are then placed between the upper cut end of the muscle and the inguinal ligament above the femoral vessels. Especial care must be observed in suturing the muscle above the femoral canal to prevent a hernia from occurring. The lateral side of the muscle is then sutured to the iliacus with a series of interrupted sutures. This is repeated on the medial side approximating the sartorius to the adductor longus.

Camper's fascia is then approximated with interrupted fine silk (Fig. 6). This maneuver will also prevent any tension on the skin edges. The skin is then approximated with fine epithelial catches which can be left in place for ten to fourteen days (Fig. 7).

A light dressing is applied and no drains are used. The patient is kept in bed for twenty-four to forty-eight hours and then allowed to be ambulatory.

RESULTS

The procedure described here has been performed on eight patients within the past two years. In one, the incision was vertical instead of parallel to the

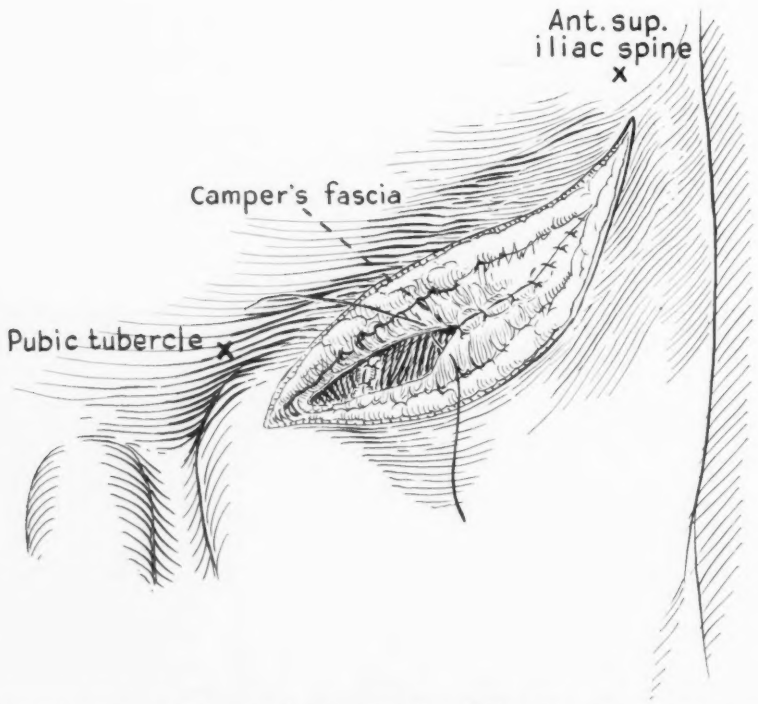

Fig. 6.—Approximation of Camper's fascia with fine 00000 silk sutures; this maneuver will prevent any tension on the skin edges.

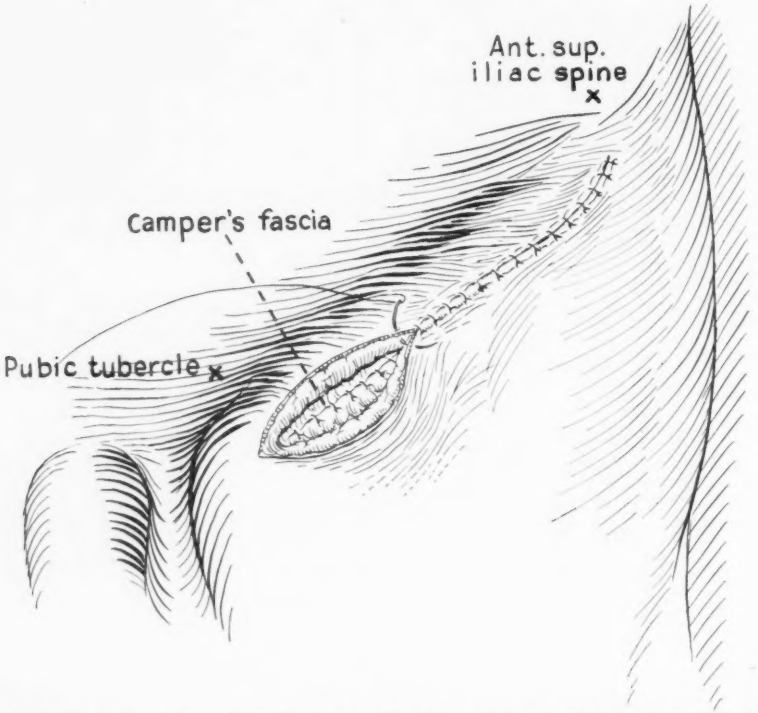

Fig. 7.—Skin being approximated with fine epithelial catches which can be left in place for ten to fourteen days.

inguinal ligament (Table I). The minimal complications associated with wound slough would indicate the efficacy of this procedure.

DISCUSSION

This procedure has not been intended for the group of nodes along the iliac vessels in the pelvis. Though this has been advocated and has been done at times by various surgeons, one questions the advisability. The iliac nodes are enclosed in a variable amount of fat and poorly defined areolar tissue and dissection is not clear. The direct communication of these nodes with the periaortic nodes even as far as the hilum of the lung makes one consider a far more radical procedure, such as that of Hinman (1919), for excision of the iliac and periaortic nodes in toto. It is a formidable operation, but perhaps should be considered in selected cases.

Fig. 8.—Photograph of the healed incision; note the fine scar that has healed by primary union.

Five of the operations were for carcinomas of the anus or lower rectum. There seemed to be adequate justification for these procedures, in view of the presence of abnormally enlarged nodes in each one of these cases. It must be emphasized again that palpation may be inadequate in discovering metastasis, as metastasis may be present without palpable lymph nodes, and that consideration to the location of the lesion, pathologic grade, and involvement of near-by organs that drain to the inguinal area, must be made. With careful pre- and postoperative management and the use of careful surgical technique, the mortality of inguinal node dissection should be no higher than that of saphenous vein ligation or inguinal node biopsy. The morbidity in this procedure, the wound of which heals less kindly than other lymph node dissections and has been due to infection and skin slough, should be almost completely eliminated.

An analysis of the cases with reference to the presence or absence of rectum as an influential factor in primary healing of wounds was also made. This has been done because the pertinent suggestion has been made that the cause of poor wound healing in inguinal node dissection is the presence of bacteria

TABLE I. INGUINAL NODE DISSECTIONS

PATIENT	SEX (AGE YR.)	PRIMARY DISEASE	BILATERAL OR UNILATERAL	SKIN SLOUGH	REMARKS
1. L. F.	F 69	Melanoma of foot	Unilateral	–	Amputation previous
2. V. B.	M 27	Melanoma of foot	Unilateral	–	Seroma; vertical incision, 150 c.c. aspirated
3. V. V.	M 20	Melanoma of heel	Unilateral	–	Amputation
4. E. M.	M 37	Ca. of sigmoid	Unilateral	–	Axillary dissection with nodes
5. R. E.	M 61	Ca. of rectum	Unilateral	–	Abdominoperineal resection
6. M. M.	F 62	Squamous cell	Bilateral	–	Seroma aspirated 70 c.c. rt. edema of legs
7. A. K.	M 66	Ca. of rectum	Unilateral	–	Combined abdominoperineal resection
8. E. C.	M 59	Ca. of rectum	Bilateral	–	Wound, separation on left; fluid underneath skin margin; no slough, healed well

draining from the anus and perianal region. However, the analysis showed that there was no significant difference between the two groups. As a matter of fact, the one patient in whom very minimal wound separation occurred had had a combined abdominoperineal resection previously (Case 8). Sermonas occurred in both groups equally (twice).

A word may be said here as to the use of the antibiotics. Two of the eight patients (both with rectum intact) were given sulfasuxidine preoperatively. The remainder received nothing. One of the two patients receiving the sulfasuxidine did so for twelve days preoperatively and twenty days postoperatively. However, in spite of this vigorous therapy, a large seroma was present. Ravdin, Zintel, and Bender (1947) have shown that oral streptomycin is much more effective against all of the common intestinal pathogens than is sulfasuxidine. Perhaps this drug may be indicated preoperatively in certain instances.

Drainage in these procedures can be dispensed with. If the lymphatics at the base of the femoral triangle are ligated with fine silk, the presence of seroma will be avoided. As experience was gained with inguinal node dissection, it was felt more and more that failure to follow this was the main cause of seroma.

SUMMARY AND CONCLUSIONS

A review of the anatomy of the inguinofemoral region is presented. The indications for the procedure of inguinal node dissection are noted. A method of inguinal node dissection is offered in which anatomic consideration to the blood supply of the skin flaps and obliteration of dead space is made. The results suggest that this method is adequate in preventing the common postoperative complication of necrosis and slough of skin.

REFERENCES

1. Barringer, B. S.: Inguinal Gland Metastasis in Carcinoma of the Penis, J. A. M. A. **106**: 21, 1936.
2. Basset, A.: Traitement Chirurgical Operatoire de l'epethelioma Primitif Du Clitoris, Rev. de chir. **46**: 546, 1912.
3. Colby, F. H., and Smith, G. G.: Carcinoma of the Penis, J. Urol. **25**: 461, 1931.
4. Coller, F. A., Kay, E. B., and MacIntyre, R. S.: Regional Lymphatic Metastasis of Carcinoma of the Rectum, SURGERY **8**: 294, 1940.
5. Dean, A. L., Jr.: Epithelioma of the Penis, J. Urol. **33**: 252, 1935.
6. Gilchrist, R. K., and David, V. C.: Lymphatic Spread of Carcinoma of the Rectum, Ann. Surg. **108**: 621, 1938.
7. Gilchrist, R. K., and David, V. C.: Prognosis in Carcinoma of the Bowel, Surg., Gynec. & Obst. **86**: 359, 1948.
8. Graves, R. C.: The Treatment of Malignant Disease of the Penis, J. Urol. **32**: 501, 1934.
9. Hinman, F. H.: The Radical Operation for Teratoma of the Testis, Surg., Gynec. & Obst. **28**: 495, 1919.
10. Lewis, F. G.: Young's Radical Operation for the Cure of Cancer of the Penis, J. Urol. **26**: 295, 1931.
11. McKelvey, J. L.: The Treatment of Carcinoma of the Vulva, Am. J. Obst. & Gynec. **54**: 626, 1947.
12. McVay, J. R.: Involvement of Lymph Nodes in Carcinoma of the Rectum, Ann. Surg. **76**: 755, 1922.
13. Miles, W. E.: Pathology of Spread of Cancer of Rectum and Its Bearing Upon Surgery of the Cancerous Rectum, Surg., Gynec. & Obst. **52**: 350, 1931.
14. Pack, G. T., and Rekers, P.: The Management of Malignant Tumors in the Groin, Am. J. Surg. **56**: 545, 1942.
15. Ravdin, I. S., Zintel, H. A., and Bender, D. H.: Adjuvants to Surgical Therapy in Large Bowel Malignancy, Ann. Surg. **126**: 439, 1947.
16. Sugarbaker, E. D.: The Surgical Problem of Cancer in Lymph Nodes, SURGERY **18**: 608, 1948.
17. Taussig, F. J.: In Obstetrics and Gynecology, edited by A. H. Curtis, Philadelphia, 1933, W. B. Saunders Company.
18. Taussig, F. J.: Primary Cancer of the Vulva, Vagina and Female Urethra, Surg., Gynec. & Obst. **60**: 477, 1935.
19. Taylor, G. T., and Nathanson, I. T.: Lymph Node Metastasis, London, 1942, Oxford University Press.
20. Young, H. H.: A Radical Operation for the Cure of Cancer of the Penis, J. Urol. **26**: 285, 1931.

Editorial

The Treatment of Salt Depletion

FROM the standpoint of the bodily economy it is important that the electrolyte osmotic pressure and reaction of the extracellular fluids be maintained within normal limits—that is, that the concentrations of sodium, chloride, and bicarbonate in these fluids all be kept at an optimum. The sodium in the extracellular fluid controls the distribution of water within the body. If its concentration falls below normal, the cells of the tissues take up water and swell, just as red blood cells do in a hypotonic solution. This leads to certain secondary disorders, the chief of which is circulatory failure.[1-5] This conduces to impairment of renal function and delay in the excretion of water as well as sodium salts. Consequently, patients with such a condition may develop edema, even when the concentration of sodium salts in the serum and extracellular fluids is low. The tendency to edema is aggravated by concomitant hypoproteinemia which may result from malnutrition or severe injury.

Such a condition of edema with hypoproteinemia and hypochloremia is most frequently encountered in patients who, having become depleted of salt by vomiting or diarrhea, are given fluids without salt to overcome the dehydration. Patients commonly present themselves for treatment in this state. Unhappily, some are still reduced to this condition by misdirected therapeutic measures. Vomiting patients are given water or other fluids without salt to drink. Water, instead of normal saline solution, is used for lavage or irrigation of the gastrointestinal tract. Glucose solutions alone or with inadequate amounts of saline solution are given intravenously. One of the commonest causes of salt depletion and edema is the lower nephron nephrosis produced by crush injuries, hemolytic transfusion reactions, and poisoning from a variety of drugs including the sulfonamides. The salt depletion in these conditions presumably arises chiefly from initial vomiting and is often exaggerated by antecedent dehydration. When the nephrosis is established, failure of tubular reabsorption and consequent leakage of salt into the urine may contribute to it.

Obviously the first consideration is the avoidance or prevention of the circumstances which produce salt depletion. The second is to include adequate amounts of salt in the fluids given to overcome dehydration. There will still remain the problem of treating a certain number of patients with edema and low serum sodium and chloride. Coller and his associates[6] have pointed out that administration of normal saline solution to such patients exaggerates the edema without restoring the concentration of sodium salts. The total quantity of such salts in the body may even be excessive. They therefore advocate the use of nothing but small amounts of glucose solution. This procedure fails, however, to rectify the deficient concentration of sodium which, because of its effect upon the circulatory state, is partly responsible for the defective elimination of water

by the kidneys. The choice of glucose solution because normal saline is ineffective cannot be logically—or physiologically—defended. It is frequently unrecognized that, although sodium salts are confined chiefly to the extracellular fluid, to raise the sodium concentration in this fluid by a given increment it is necessary to give enough sodium to increase its concentration in the total fluid of the body (both extracellular and intracellular) by this amount. This follows from the fact that the cell membranes are freely permeable to water. When the osmotic pressure of the extracellular water is raised by the addition of salt, enough water passes from cells to extracellular fluid to restore osmotic equilibrium between the two compartments.

Assume a patient with a total fluid volume of 60 liters, of which 20 is extracellular, and assume that this extracellular fluid contains 120 millimols per liter of sodium, instead of the normal 135. To raise this concentration from 120 to 135 millimols in the extracellular fluid alone would require $15 \times 20 = 300$ millimols of sodium. However, since there would be the transfer of water mentioned previously, the amount actually required would be $15 \times 60 = 900$ millimols of Na. This is approximately the quantity found in 6 liters of normal saline solution, containing 150 millimols per liter. To secure the desired effect, however, the salt would have to be introduced in the dry form. Introduction of 6 liters of 150 millimolar saline solution would increase the sodium concentration of 60 liters of fluid from 120 millimolar only to 123 millimolar. To raise the concentration from 120 to 135 millimols with normal saline solution would require 60 liters of fluid. It is clear from these calculations why Coller and his associates increased only the edema without raising the serum sodium in their patients by injections of normal saline solution. Their failure did not justify the inference that sodium chloride is contraindicated in the treatment of edema with hyponatremia. It was not the salt that was at fault, but the large amounts of water in which it was dissolved. Normal saline solution in proper quantities is appropriate for the maintenance of patients in a state of adequate hydration with normal serum electrolyte patterns. It is the fluid of choice for patients who are dehydrated. But for the correction of serum sodium deficit in the presence of an adequate supply of fluid or edema, hypertonic (3 to 5 per cent) salt solution should be given. By this means the introduction of large volumes of fluid can be avoided. If the heart is competent, such treatment, by overcoming the circulatory insufficiency that accompanies hyponatremia, will promote diuresis and elimination of the edema. It may be supplemented by glucose solution, but again the glucose should be given in concentrated form (10 per cent). It is objected that hypertonic solutions are likely to cause venous thrombosis. This can be avoided if care is taken to preserve a free flow of blood in the vein by the use of a small needle so inserted and fixed that there is no obstruction to blood from the more distal part of the vein. It should be unnecessary to add that it is futile to inject salt solution of any concentration if precautions are not taken to prevent wastage of salt by other channels. Transfusions and other measures for the support of the circulation must not be neglected.

Proper regulation of the salt intake, especially when hypertonic solutions are employed, should be controlled by frequent analyses of the serum. Until suitable flame photometers become available, it will be necessary to estimate sodium by inference from the concentrations of bicarbonate and chloride. Inclusion of sodium will permit more precise regulation.

REFERENCES

1. McCance, R. A.: Proc. Roy. Soc., London, **119**: 245, 1936.
Idem: Lancet **2**: 190, 1938.
2. Danowski, T. S., Winkler, A. W., and Elkinton, J. R.: J. Clin. Investigation **25**: 130, 1946.
3. Elkinton, J. R., Danowski, T. S., and Winkler, A. W.: J. Clin. Investigation **25**: 120, 1946.
4. Danowski, T. S., Winkler, A. W., and Peters, J. P.: Yale J. Biol. & Med. **18**: 405, 1946.
5. Elkinton, J. R., Winkler, A. W., and Danowski, T. S.: J. Clin. Investigation **26**: 1002, 1947.
6. Coller, F. A., Campbell, K. N., Vaughan, H. H., Iob, L. V., and Moyer, C. A.: Ann. Surg. **119**: 533, 1944.

—*John P. Peters, M.D.*
New Haven, Conn.

Recent Advances in Surgery

CONDUCTED BY ALFRED BLALOCK, M.D.

HEMORRHAGE INTO THE BILIARY TRACT FOLLOWING TRAUMA—"TRAUMATIC HEMOBILIA"

PHILIP SANDBLOM, M.D., M.S., STOCKHOLM, SWEDEN

(From the Surgical Department of the Örebro Hospital)

HEMORRHAGE into the biliary ducts as a result of trauma to the liver region has previously been observed only in rare cases. With reference to one of these Wright and associates[34] mentioned that in central rupture of the liver, blood, because of its entrance into the biliary tract, may appear in the vomitus. In his comprehensive monograph on injuries to the liver and biliary ducts, Thöle[31] dismissed the matter with the following sentence: "Bloody stools are a very rare early symptom, and only those are of interest in this connection." Other authors as Andersson,[2] Bauer,[3] Brandberg,[4, 5] Castrén,[6] and Vance[32] do not even mention the condition, which would thus appear to be very rare.

The object of this work is to study the symptom of hemorrhage into the biliary tract, its frequency, and its character. It will be based on a critical review of the literature. The subject was brought up by the following case observed in the Örebro Hospital.

CASE 1 (Örebro Hospital, No. 3474/1936).—A previously healthy boy, 7 years of age, was admitted to the surgical service. Ten days prior to admission he had while bicycling received a hard blow from the handle bar over the right lower part of the chest. He immediately felt severe pain at the site of the blow and became very pale. These symptoms abated after about thirty minutes. Some hours later he again had severe pains in the right flank, and pallor. He was examined at the Dispensary and a bruise was found at the site of the blow, but nothing pathologic was observed. Two days later there was a renewed spontaneous cramping in the right flank, and chills. Afterward he was confined to bed with an evening temperature of about 38.5° C. He had a cough during the first week. Ten days after the trauma there was renewed, rather severe colicky pain in the right flank and, in addition, marked pallor and yawning. He was referred to the hospital.

Examination.—The general condition was good. He was afebrile, had a slight anemia with 60 per cent hemoglobin, red cell count 3,600,000, white cell count 13,800, sedimentation rate 38. Urinalysis revealed urobilinogen reaction negative, urobilin markedly positive. The abdomen was soft and not distended. The right flank was tender. At the right lateral rectus border immediately below the thorax there was a rounded mass the size of a pigeon's egg. Roentgen examination of abdomen, chest, and colon showed nothing pathologic. It was considered likely that the patient had a retroperitoneal hematoma. This opinion was supported by the well-defined tenderness of the right flank with absence of symptoms from the rest of the abdomen, and by the anemia and the leucocytosis. In the evening the patient again had severe pains at this site.

Operation.—Cholecystotomy and drainage were carried out.* Incision was made at the right lateral rectus border above the umbilicus. Liver, kidneys, and bowel had a normal

*Operation performed by Professor G. Bohmansson, surgeon-in-chief.

appearance. There was no peritonitis, and no free blood in the abdomen. The gall bladder was distended, glistening blue, and firm. It could not be evacuated by means of digital compression. Dark brown blood was obtained on puncture. The gall bladder, however, could not be emptied by this measure, wherefore it was incised. By means of aspiration a firm blood clot the size of a hazlenut was removed. No source of the hemorrhage was found in the gall bladder. This was sutured and the abdomen was closed.

The wound healed without complications. During the first days after the operation Weber's test for blood in feces was markedly positive, but six days later it was negative. After one week the patient was discharged free from discomfort. Three weeks later he was reported entirely well with absence of symptoms. Repeated tests for blood in the stools during this period were negative. Twelve years later it is reported that the patient subsequent to the operation has never had any discomfort from the liver or the biliary ducts.

Comment.—As a result of the distinct trauma toward the hepatic region there occurred in this case a hemorrhage into the biliary tract. At operation performed ten days after the trauma, liquid and coagulated blood were found in the gall bladder. No source of the hemorrhage could be observed, however. In the further course blood was for some time demonstrated in the stools.

The symptoms that occurred may be explained by this hemorrhage. The pallor and yawning were the expressions of a slight shock and a moderate secondary anemia. The pyrexia may have been caused by resorption of the blood. The attacks of pain, which had the character of biliary colic, were probably brought about by the presence of coagula in the biliary tract.

Before entering upon the discussion of the source of the hemorrhage I wish to describe a case, very similar to the present one, reported by Siegel[30] in 1909.

CASE 2.—A 32-year-old man on a bicycle fell with his right side against the handle bar. He immediately felt severe pain at the site of the blow but was able to get home unassisted. A physician found multiple fractures of the ribs on the right side and blood in the right pleural cavity. Soon the patient felt better but on the eighth day he had severe attacks of abdominal pain which were not relieved by large doses of morphine and opium. Not until the tenth day, when a long coagulum was passed per rectum, was the distress relieved. On the twelfth day there was renewed abdominal pain and a temperature of 38.6° C. On the fourteenth day there was a condition of collapse with renewed severe colicky pain.

At examination the patient was found to be slightly icteric. Marked dullness on the right side from the level of the mamilla merged over into the liver dullness which reached down to the anterosuperior spine. Below the hepatic dullness a mass was palpated. On puncture of the right pleura a small amount of blood was obtained. The lung was encountered already at the depth of 2 cm.

Operation.—At laparotomy a small amount of blood was found in the abdominal cavity. The gall bladder was enveloped in the omentum. When this was loosened the gall bladder was found, with a blackish-green discoloration and distended to the utmost. In the fundus there was found a gangrenous spot the size of a pea which had been covered by the omentum. When this was loosened a foul-smelling fluid with blood clots and bile pigment escaped from the gall bladder. The gall bladder was extirpated. On the lower surface of the liver there were found a number of ruptures up to the length of 4 cm. A drainage tube was laid against the pedicle of the extirpated gall bladder.

Two weeks following operation a considerable amount of blood was drained from the wound. In connection with this the patient had a severe attack of pain and two days later he was again icteric.

A flow of bile from the wound which had commenced immediately after the operation ceased at the beginning of the attack of pain. It was assumed that a blood clot had found its way into the hepatic and the common duct, giving rise to bile stasis with jaundice.

The patient gradually recovered entirely, without further measures.

Siegel assumed the course to be as follows: The blow from the handle bar in addition to the fracture of the ribs and the rupture of the liver caused a contusion of the gall bladder. In consequence of this contusion a hemorrhage to the gall bladder occurred. On the eighth day a blood clot occluded the cystic duct and gave rise to the severe attack of pain in the same manner as the passage of a stone. When the coagulum had passed and had been evacuated per rectum there appeared a temporary improvement. A renewed impaction of a coagulum occurred and infection from the bowel supervened, whereby the conditions prerequisite for distention gangrene arose.

The rarity of such a course was ascribed by Siegel to the fact that the trauma must be accurately balanced—a slighter trauma does no damage, and a more severe trauma causes total rupture of the gall bladder. Siegel pointed out that the case is of particular interest in that it shows that a blood clot may have the same sequelae as a gallstone: colicky pain, inflammation, and gangrene.

Comment.—The history of the present case (Case 1) and that of Siegel (Case 2) were very similar—even the trauma was identical. In the case of Siegel, however, the gall bladder was gangrenous by the time of the operation. As to the cause of the gangrene, it could either be a direct effect of the trauma or, more likely, the effect of distention of the gall bladder caused by an impaction of coagula.

DISCUSSION

It was in both instances considered that the hemorrhage emanated from a lesion in the mucosa of the gall bladder.

According to my opinion, however, this is not certain. The blood may also have come from a *central rupture of the liver* and have been carried to the gall bladder through the biliary ducts. This hypothesis is supported by the following facts. In Case 1 no source of the hemorrhage was found at inspection of the interior of the gall bladder. In Case 2 the gangrenous part of the gall bladder which was supposed to have been the source of hemorrhage was situated in the fundus where the blood vessels are smaller than in any other part of the gall bladder. On the whole it is unlikely that the small vessels of the gall bladder or the external bile ducts which might be concerned would give rise to such profuse and protracted bleeding. In the thirty odd cases of total rupture of the gall bladder or the external bile ducts reported in the literature the bleeding has in all instances been insignificant, provided that there has not been concomitant damage to the liver (Rudberg,[28] Norgore,[22] and Lewerentz[18]).

In Case 2 it appears as though the bleeding had continued after the removal of the gall bladder, because blood emptied through the wound two weeks later. This blood may, of course, also have come from a hematoma in the operative region but the simultaneous obstruction of the hepatic duct makes it more probable that it emanated from the liver.

A central rupture of the liver would satisfactorily explain the protracted hemorrhage, as the thin-walled vessels of the liver parenchyma have but slight power of contraction.[8] The external ruptures found by Siegel on the lower

surface of the liver are similar to those frequently found by Hämäläinen[14] concomitantly with central ruptures.

On the basis of this line of argument I consider it highly probable that the hemorrhage in the two cases described arose from a central rupture of the liver. The following very interesting case reported by Hawthorne and associates,[11] from the American Hospital for Disease of the Stomach, not only supports this conclusion but also throws considerable light on the whole subject.

CASE 3 (No. 21464).—In 1941, a truck rim blew off, striking the anterolateral chest wall, upper abdomen, and face of a man. He was given immediate treatment for shock, fractured seventh and eighth ribs, and fractured nose. The injury to the thoracic cage masked the intra-abdominal injury so that it was not recognized at this time in spite of hematemesis on two occasions and tarry stools which were noticed by the patient. After seven weeks of hospitalization he was discharged and returned to work nine weeks after the date of injury. Two weeks later while at work he felt a sudden sense of suffocation with severe pain in the upper abdomen but most marked in the gall bladder area. He vomited a large amount of blood and there was gross blood in the stool.

Upon admission, fourteen weeks after the injury, the red cells were 2,790,000 and the hemoglobin 47 per cent. All physical findings were negative. By the use of blood transfusions and intravenous glucose he improved to the extent that the red cell count was 4,190,000 and hemoglobin 70 per cent. During this time, however, he vomited on three occasions a very thick black material which on examination proved to be a mixture of blood and bile. The patient was allowed to go home two months after admission, still showing a trace of occult blood in the stool.

He was readmitted to the hospital three weeks later and plainly showed the effects of a severe hemorrhage the night before. During the three weeks at home he had several attacks, consisting of a sense of tightness in the liver area and severe colicky pain followed by nausea and vomiting of the same thick black material that had been examined in the hospital. He also passed this same type of material by bowel. A large defect in the pyloric end of the stomach was demonstrated by x-ray examination.

Operation.—An upper right rectus incision revealed a mass of adhesions over the gall bladder and duodenal areas. No ulcer was demonstrable, but in view of the large amount of hematemesis it was deemed advisable to open the duodenum. The usual Heineke-Mikulicz incision was made. No definite ulcerated areas were found, but several small congested areas in the mucosa were touched with the cautery and the incision was closed transversely. This did not explain the bleeding and, on releasing the dense adhesions, the gall bladder was found to be very dark in color, to be enlarged, and to contain a smooth hard mass the size of an egg. The gall bladder was removed and the bile ducts were explored through the patulous cystic duct. Some very dark material of the same type that he had vomited was found, but there was no evidence of tear of the ducts or liver. The large mass in the gall bladder proved to be inspissated blood and bile.

He made an uneventful postoperative recovery and was discharged on the sixteenth day. The stool was negative for occult blood.

One week later he had another attack of colicky pain in the subhepatic area lasting one hour and vomited a small amount of the very dark material that had been observed on previous occasions. A large amount of green-black fluid was passed by bowel. There followed a number of these short attacks at intervals of a few days. During the last attack a branching clot which appeared to be a cast of the hepatic ducts was vomited. This proved on examination to be inspissated blood and bile. Since then he has been entirely free of all the former symptoms and at present is in excellent health.

Hawthorne concluded that in all probability there was in this case a cavity and hematoma deep in the substance of the liver that continued to necrose

and bleed through a large biliary duct until healing finally occurred. He could not give any other explanation for the continued bleeding through the biliary channels.

Comment.—Case 3 is so similar to Cases 1 and 2 that it seems highly probable that they have the same cause. In Case 3, however, the hemorrhage certainly could not have come from the gall bladder, as it continued for weeks after cholecystectomy. It must have come from the interior of the liver.

In all likelihood the three cases demonstrate the effect of hemorrhage into the biliary tract originating from a central rupture of the liver. Before discussing the different aspects of the symptom a short account will be given of this special type of injury.

CENTRAL RUPTURE OF THE LIVER

Liver lesions may be divided into the following groups (Brandberg[4]):

1. Ruptures through the capsule and the parenchyma
2. Subcapsular lesions:
   (a) Subcapsular hematoma
   (b) Subcapsular rupture
   (c) Central ruptur (term introduced by Wilms[33])

Krogius[16] suggested and Hämäläinen[14] proved in experiments that most central ruptures of the liver are caused by compression of the inelastic and fragile liver parenchyma. A tear occurs, veins and bile ducts rupture, and a cavity filled with blood and bile is formed.

By careful examination of a series of autopsies, Bauer[3] could show that central ruptures of the liver are not infrequent—they probably occur at least as often as ruptures through the capsule. Because of their location in the interior of the liver they do not give rise to the hemorrhage and bile leakage into the peritoneal cavity which generally is such an alarming symptom of ruptures through the capsule. While the liver capsule is very sensitive, the parenchyma itself has few sensory nerves.

Those are the reasons why central ruptures give such vague symptoms, if indeed any at all, and therefore often escape diagnosis. Some of them may heal with scar formation without complications, others produce cavities filled with blood and bile and may later give rise to liver abscesses.

Symptoms of central liver ruptures may appear early or late (Andersson[2]).

Early symptoms:

1. *Contusion* of the wall of the chest or the abdomen.
2. *Shock.*

   Those two symptoms of course are unspecific.

3. *Pain.* Most authors agree that true central ruptures are painless unless a cavity is produced sizeable enough to enlarge the liver.[8] A dull, aching pain irradiating through the shoulders, generally the right one, is then a sign of the tension of the capsule. If the cavity breaks through to the capsule the pain becomes more intense.

4. *Signs of bile in the blood and the urine.*

A *bradycardia* caused by bile salts in the blood seems to be a rather uncertain symptom. Finsterer[9] stressed the importance of this symptom but later authors as Wright and associates[34] have not been able to find it.

Jaundice may be caused by the resorption of bile from the cavity or may be the result of an obstruction of the biliary ducts. Castrén[6] has demonstrated the presence of leucine crystals in the urine.

5. *Enlargement of the liver* is dependent on the size of the cavity formed.

6. *Secondary anemia* seldom becomes pronounced.

7. *Embolism* to the heart and lungs is a serious complication in some cases. It is caused either by pieces of liver tissue or fat from the liver cells which enters the circulation via the hepatic veins.

Late symptoms:

An enlargement of the liver and also jaundice may appear some time after the lesion.

8. *Fever* is generally a sign of resorption from the intrahepatic hematoma. It can also be a sign of infection in the cavity with the formation of an abscess. Liver abscesses often are sequelae of intrahepatic hematomas.

"HEMOBILIA"

If the essential cause in the three cases described was a central rupture of the liver, which seems highly probable, the list of symptoms of this type of injury could be supplemented with that of hemorrhage into the biliary tract. This symptom may be compared to the hematuria which results from damage to the kidneys and accordingly termed "hemobilia."

"Hemobilia" might be expected in all types of liver injuries, but it should be more prominent in the central ruptures for the following reasons:

1. Patients with ruptures through the capsule generally die or get treated so short a time after the trauma that a "hemobilia" would not make itself evident. When the capsule is torn, there will be less resistance to the blood flow into the peritoneal cavity than into the biliary tract.

2. In central ruptures more and larger biliary ducts are apt to tear than in superficial ones. This will facilitate the escape of blood into the biliary tract. In subcapsular hematomas there might not be any lesion of the biliary tract at all. It is suggestive that most of the cavities formed by this type of lesion contain blood without bile.

Whereas a hematuria, at least when macroscopic, is a very striking symptom, a "hemobilia" is apt to be overlooked if it is not so profuse that it causes bloody vomit or tarry stools.

In the course of hematuria the formation of blood clots usually gives more alarming symptoms of urinary colic or obstruction. The same should be expected in the biliary tract where clots would cause biliary colic and occasionally obstruct the ducts with risk of jaundice. It should be remembered that the bile has an inhibitory effect on the clotting of blood, which should decrease the number of cases with this complication.

The three cases described give examples of all these happenings. In Case 3 there was blood in the vomit and all three patients had blood in the stools. There was marked biliary colic in all three and in Case 2 there was transitory jaundice.

REVIEW OF CASES

The cases of subcapsular liver lesions reported in the literature have been examined with special attention to symptoms suggesting "hemobilia." This has met with the following difficulties:

1. The case histories are often incomplete and give too scanty information on the necessary points. Some cases with "hemobilia" might therefore escape recognition.

2. The symptoms when found can often be due to other causes than "hemobilia." In fact most authors have given other explanations. Bloody vomit and stools may be caused by concomitant lesions of the digestive tract or by swallowed blood. Pain may emanate from a capsule in a state of tension or irritation. Jaundice may be due to resorption of bile from a cavity in the liver, etc.

3. The diagnosis of central liver rupture is often uncertain, especially if operation or autopsy has not been performed. Even after operation it is often difficult to decide whether it is a case of true central rupture or subcapsular lesion.

I have found forty cases where with different degrees of probability a central rupture of the liver occurred. In nine of these the patient died on the first day and in another two within the first four days.[3, 10, 21] In nine others the information is too scanty to allow any estimation.[3, 6, 15, 20, 24, 29] This leaves twenty cases where the problem in question may be studied. In eleven cases no signs of hemobilia are described.[1, 2, 5, 7, 13, 17, 25-27, 31] (In five of these, however, there are reasons to believe that the lesion was subcapsular[7, 17, 25, 26]). In the remaining nine cases there were signs indicating a hemorrhage into the biliary tract. Three of them were reported herein as Cases 1 to 3. The rest of these cases have been divided into groups according to which main sign of "hemobilia" they present: hemorrhage or biliary colic.

Cases With Hemorrhage.—Cases 4 to 6 (also Cases 1 to 3) had hemorrhage. Case 4 was reported by Owen[23] in 1848.

CASE 4.—A man 22 years of age fell from a wagon. He had an immediate state of shock and complained of pain in the stomach. Seen two hours later, he was then in deep shock. There were no signs of injury on the trunk. The next morning he was better, but complained of pain in the right shoulder, which was not damaged. He had soreness over the region of the liver extending up the back of the chest. He was short of breath and could lie only on the left side. When he tried to turn the pain became worse, especially in the shoulder.

The third day the attacks of pain were less. There was some jaundice. On the fourth day he had paroxysm of pain two or three times, but not so much pain on pressure over the abdomen. The jaundice had increased.

On the sixth and seventh days, the stools contained mucus and bright blood. The jaundice was increasing. He got a troublesome hiccup which continued on the eighth day. Epistaxis occurred two or three times. In the evening of that day, he passed a motion consisting of nearly one-half pint of dark grumous blood.

Even on the ninth day the motions consisted of dark colored bloody fluid. There was no more hiccup. The jaundice was decidedly less. The countenance was cheerful. There was no pain and the dullness over liver did not extend very high. A favorable prognosis was given.

On the tenth and eleventh days there was very little urine. The face looked pinched, the pulse was easily compressed, and the abdomen was distended.

On the twelfth day he was delirious; hands and thumbs were twittering. In the afternoon while his head was being raised, he was seized with general convulsions and ceased to breathe within five minutes.

Autopsy.—There was no blood in the peritoneal cavity. There was no peritonitis. The liver was much enlarged and there were some soft adhesions between its convex surface and the diaphragm. When taken out, a laceration was seen extending across its right lobe. At the back of the laceration, which extended deeply into the lobe, there was a collection of fluid and clotted blood. No connection between this and the intestines was found. No other lesions of any importance were discovered.

Owen discussed the case at length. Only his comments on the hiccups and the melena will be related:

> The hiccup, another not unusual symptom of affections especially of the diaphragmatic surface of the liver, did not appear until about the sixth day after the injury, and, although severe and urgent while it lasted, was not of long continuance. Did this symptom, so often an accompaniment of inflammatory action about the surface of the diaphragm and liver, mark the period of formation of the soft adhesions found connecting the diaphragm and liver; or did it depend on some temporary increase of upward pressure only, and become relieved by the evacuation of the grumous blood, as it began to disappear when this took place?
>
> Although probably the mucosanguineous discharges from the bowels were chiefly due to the remedies employed, yet from the facility with which they were brought on, and the frequent attacks of epistaxis, there probably existed a more or less congested state of the mucous membrane throughout: in regard to the large discharge of blood on the evening of the eighth day, viewing as I then did, the case as one of general concussion, with congested state of liver, I had hoped it would have proved a salutary or critical discharge; for it will be noted that not only the hiccup, until then distressing, ceased about this time, but the countenance and manner became cheerful, the jaundice less, the dullness of the right side of chest diminished, and the patient expressed himself relieved. Not being able to detect any direct communication between the intestine and the liver, I am still inclined to think it must have suddenly regurgitated from the portal vessels, and, but for other conditions present, might have relieved or removed the congested state of liver.

Comment.—Owen's case was admirably well studied and commented. It is regrettable that space does not allow it to be related in full.

The death in his case was probably caused by shock due to the liver injury and secondary anemia. The type of pain with irradiation through the right shoulder and with relief when lying on the left side is typical of a lesion close to the capsule. The paroxysms of pain on the fourth day when there was not much pain on pressure over the abdomen could have been caused by blood clots in the biliary tract.

The source of the copious melena could hardly have been the epistaxis which is not described as being serious. There was no hematemesis and the blood did not show signs of having been digested in the stomach. As there was no other lesion in the digestive tract the blood probably originated in the liver.

Owen himself discussed the connection between the melena and the improvement of the patient, characterized by the disappearance of the hiccup, the decrease of jaundice, the diminished pain, and the reduction in size of the liver. As he thought that there probably was a connection he looked for a direct communication between the cavity in the liver and the intestines.

With the experience gained from Cases 1 to 3 there does not seem to be much doubt that the communication which Owen looked for in vain was the biliary tract and that the melena was a sign of hemobilia.

Hitzrot[12] reported the following case from The New York Hospital, in 1908.

CASE 5.—A man aged 32 years was admitted. He complained of swelling in the upper part of the abdomen, weakness, pain in the abdomen radiating to the left side and into the back below the left shoulder blade, and blood in the stools.

Four months before admission the patient had been struck, while at work, a severe blow upon the stomach by a truck stay. Following the blow he was nauseated, felt weak, and had severe abdominal pain, for which he consumed large quantities of whiskey. He was unable to work as the pain was aggravated by moving, coughing, vomiting, or deep breathing. About two months after the injury the pain became more intense, was localized definitely in the epigastrium, and the patient could neither lie down nor sleep. About three months after the injury a swelling appeared which thereafter steadily increased in size. Throughout, he had morning vomiting which never contained blood.

Examination.—The general examination was negative. The abdomen was markedly swollen in the epigastric region, where there was a large tender mass extending from the costal margin almost to the navel and laterally about five inches each side of the median line. The mass seemed elastic, semifluctuant, and quite superficial. It was continuous with the liver dullness. The stools contained blood once. Hemoglobin was 72 per cent. The temperature ranged from 99° to 101° F.

Operation.—A median epigastric incision was made over the center of the mass, exposing a large cystic mass projecting from the liver surface. On aspiration with a trocar, 82 ounces fluid blood were obtained, the removal of which left a large cavity which extended deeply into the surface of the liver. This cavity was packed with two large one-yard gauze rolls. The other viscera felt normal. Convalescence was uneventful and the patient was discharged from the hospital at the end of six weeks. Four months after the operation he was reported as free from pain. Stools were normal and he again resumed work.

Hitzrot comments: This case presents many features of interest, namely, the long period of symptoms, the gradual appearance of the swelling, the marked alcoholic history, the size of the blood cyst and the long period (five months) which elapsed between the injury and the operation.

The case represents the type of subcapsular hematoma of some size forming a blood cyst.

Comment.—There was probably a subcapsular rupture in this case which produced a subcapsular cavity through a gradually increasing collection of blood. As in the preceding case the pain was of the kind that usually emanates from the capsule.

The symptom of bloody stools is just mentioned, but it seems to have been one of the chief complaints of the patient when he entered the hospital four

months after the accident. During his hospital stay the stools contained blood once. The protracted hemorrhage can in this case best be explained as caused by the liver lesion.

The following case was reported by Wulsten[35] from The Surgical Department of the Hindenburg Hospital in Berlin in 1931.

CASE 6.—An 11-year-old girl was admitted to the hospital.

History.—Four weeks before admission while she was coasting, her sled had run into a fence. She received a severe blow in the upper abdominal region. She began to vomit and complained of severe pain in the whole body. She was brought to her home where she became unconscious and vomited frequently. She was bruised over the regions of the liver and the spleen. The next day as the child had repeated nosebleeds a nose specialist was called who treated the hemorrhage with cautery. For a few days she was better but was not able to leave the bed. She became increasingly pale and weak but had no fever. Eight days before admission the nosebleed recurred. She vomited light blood both then and six days later. She could not lie on the right side.

Examination.—The patient was an extremely pale and emaciated looking 11-year-old girl. There was some tenderness over the liver and the spleen. The liver could be palpated 4 cm. below the costal arch.

The child lay steadily on the left side and did not want to turn over on her back. The urine contained many red blood corpuscles. Hemoglobin was 27 per cent. It was supposed that she had a central liver rupture, possibly a portal thrombosis. The child was treated for two months before she died.

Now and then the temperature rose to 39.5° C. for a few days. During these days the pain in the liver region became worse and she vomited frequently. During the three first weeks the stools were tarry from blood, often diarrhea. After two weeks the hematuria disappeared. The anemia could not be influenced and the hemoglobin sank to 19 per cent. The liver region remained tender but the lower border of the liver was palpated at different levels. For a short time the child was in better condition but then she again had severe pain in the liver region. From that time on she went rapidly downhill and had unbearable pain until she died.

Autopsy.—At autopsy the following was found: In the right lobe of the liver there was a cavity the size of a child's head, covered by the right diaphragm. The liver capsule was intact. The cavity contained blood clots and brownish-red fluid.

There were multiple subpleural and subepicardial ecchymoses. There also were numerous small hemorrhages in the mucosa of the small intestine and solitary ones in both kidney pelves.

Microscopic sections of the liver showed both old and recent necrotic areas. In the center of the latter there were signs of fresh hemorrhages.

Wulsten comments: A long-standing hematuria and blood in the stools for weeks with tarry stools as late as five weeks after the injury have never been described. These signs can perhaps be of help in the diagnosis.

Comment.—The liver rupture in this case gave rise to a large cavity. The type of pain was similar to that in Case 4 and indicates that the lesion had a subcapsular location from the start. Judging from the outcome of Cases 5, 7, and 8 where the cavities were of similar size, the child could perhaps have been saved by an early operation with drainage of the cavity.

The striking features in this case were the marked anemia and the protracted hemorrhage. At autopsy there were found multiple subpleural and subepicardial ecchymoses, numerous small hemorrhages in the mucosa of the small

intestine, and solitary ones in both kidney pelves. These were supposed to be of toxic origin. Another possibility is that they were caused by the sudden increase in the venous pressure when the thorax was compressed.

The blood in the vomit and in the stools could have originated from these hemorrhages in the mucosa. Considering the large amounts of blood that were lost and with the experience gained from Cases 2 and 3 it seems more likely that the blood came from the liver lesion. The changes in volume of the liver that are described could have been due to evacuation of blood through the ducts alternating with hemorrhage from the wall of the cavity.

Cases With Biliary Colic.—Cases 7 to 9 (also Cases 1 to 4) had biliary colic. Such a case was reported by Holm[13] at the Surgical Department of Geh.-Rat Bier in Berlin in 1914.

CASE 7.—A 19-year-old laborer was admitted after having been run over by an automobile while bicycling. He was in a state of severe shock on admission. He had a fracture of the left forearm and also an extraperitoneal rupture of the bladder, which was operated upon.

After an improvement of a few days he suddenly had an intense pain below the right costal margin, radiating to the right shoulder. No explanation was found in the chest for this pain. The abdomen was soft and not tender. The piercing pains continued for a few days but then there appeared a marked tenderness to pressure over the liver with reflectory abdominal rigidity.

Two weeks after the accident his condition became worse. He became icteric and had violent attacks of vomiting. The liver region remained just as tender but it was also noted that the liver was markedly enlarged.

Operation.—Operation was then carried out. There was no blood in the abdominal cavity and no peritonitis. The liver was enlarged to twice the normal size and the convexity distended like a balloon (the biliary ducts are not described). Upon puncture of the liver a cavity was found below a more than 2 cm. thick layer of parenchyma. From this 3 liters of fluid, consisting of bile and blood, were emptied, after which the liver collapsed. The cavity was drained; in the beginning there was abundant secretion but six weeks later the wound was healed. The patient recovered.

Holm concluded that this was a case of central rupture of the liver, noteworthy because of the unusual amount of bile mixed with blood that was found in the cavity.

Comment.—In this case there was undoubtedly a central rupture of the liver with an accumulation of bile and blood. The severe pains below the right costal margin radiating to the right shoulder had a definite character of biliary colic. They can hardly be explained by the swelling of the liver with distention of the capsule, as the abdomen then was entirely soft and not tender. The tenderness did not appear until after several days, and the signs of hepatic enlargement appeared still later. The course in this case is best explained by the presence of blood clots in the biliary tract.

The following case was reported by Brandberg[4] from the Lund Hospital in 1926.

CASE 8 (No. 2692).—A boy aged 14 years was knocked down by a bus and was hospitalized on the following day. On admission a right-sided fracture of the olecranon was established and was operated upon. There was some tenderness in the right side of the abdomen from the navel up into the epigastrium. There was a fracture of the pelvis and

lesion of the right kidney (tenderness to pressure over the kidney and hematuria). These lesions healed without complications. The patient had a slight increase in temperature. The tenderness in the abdomen declined and the hematuria disappeared. Some days after admission the patient had attacks of sudden pain, radiating from the epigastrium out to the left shoulder. The attacks lasted five to ten minutes, came on several times a day, and were frequently so severe that the patient groaned aloud. Between the attacks of pain the patient had no discomfort. Gradually the attacks occurred more seldom, but on the other hand the patient began to complain of a continuous sensation of tenseness in the epigastrium. There was a concomitant increasing enlargement of the liver, the liver finally reaching the level of the umbilicus. Urine and feces were normal in color. No icterus was observed.

Operation.—Laparotomy was performed one month after the accident. The greatly enlarged liver showed no external lesions but fluctuated markedly. After isolation of the abdominal cavity the liver was incised and at the depth of 1 cm. a cavity was found which was seen to contain 3 liters of bile. Drainage was carried out. The first days following operation the feces were entirely acholic and an abundant amount of bile flowed out into the bandages. The bile flow soon ceased, the feces regained a normal color, and about six weeks postoperatively the patient was discharged, entirely cured.

I have learned from the hospital that the feces were not examined for blood until the time of the operation, that is, after the attacks of pain had ceased. The tests were then negative.

Brandberg discussed the intense pain in his and Holm's patients (Cases 8 and 7). The difference in the irradiation—in Holm's case through the right shoulder, in his own through the left shoulder—he explained by the fact that in the first case the rupture was mainly in the right part of the liver, in the second case in the left part. Brandberg found that those two cases are arguments against the general applicability of the rule that central ruptures of the liver do not cause pain.

He concluded that the distention of the liver is more important as a cause of pain than the localization of the lesion.

Comment.—Brandberg's case was very similar to Holm's and was also a case of true central liver rupture. The attacks of violent pain of short duration with intervals free from discomfort can best be explained by the passage of blood clots. The only atypical trait is the irradiation through the left shoulder.

It is difficult to understand how these attacks could have come from a distention of the capsule because the patient was free from symptoms between the attacks. The liver did not become enlarged until later. Then there also was a continuous sensation of tenseness in the epigastrium such as one would expect from a distended capsule.

This case history seems to demonstrate clearly the difference in pain occasioned by the passage of clots as compared to the pain from a distended capsule, both occurring successively in the same case.

Castrén[6] of The Hospital of the Red Cross of Finland described the following case in 1946.

CASE 9.—A 14-year-old boy was knocked down by an automobile and was pushed 10 meters by one of the front wheels. He could walk alone about 500 meters but after a few hours he could not move and could not even lie on his back. His comrades brought him to

the hospital. He was then in a state of shock but was perfectly conscious. He had bruises on the right elbow, on the right side of the pelvis, and on the lower part of the costal margin. There was tenderness in the right side of the back, corresponding to the lower ribs. There was macroscopic hematuria which disappeared on the third day. The hemoglobin was 49 per cent. On the fourth day he was discharged with the diagnosis of abdominal contusion (rupture of the right kidney?).

He stayed in bed at home and everything was well until the eighth day, when he felt a pain in the right lower part of the chest increasing with the respiration. On the tenth day he had such violent pains in the epigastrium that he doubled up and was short of breath. At the same time there was increasing tenderness in the back. He was then brought to the hospital again.

At examination he looked ill; he was pale and the hands and feet were cold. There was tenderness in the abdomen, especially under the right costal arch. Hemoglobin was 60 per cent. The urine contained albumin, some hyaline and granulated cylinders, and leucine crystals. At x-ray examination the right diaphragm showed decreased excursions.

The pains decreased at first but on the sixteenth day he had a violent attack of severe pain irradiating through the right shoulder. The liver, of firm consistency, could be felt in the mamillary line, two fingerbreadths below the costal arch. At that point there was extreme tenderness. Hemoglobin was 58 per cent, temperature 38.2° C.

Ten days later the pains had disappeared; there had been no fever for one week. The liver was unchanged. One month later he was back at work without symptoms. The diagnosis was central rupture of the liver.

Castrén was fairly certain that there was a central rupture of the liver in this case. Besides the story and clinical signs there was also biliary pigment in the urine, indicating liver damage. The finding in the urine of albumin and cylinders made him believe that there also was a hepatorenal syndrome. He did not discuss the pain in this case. I wrote to the hospital and found that the stools were not examined for blood.

Comment.—In this case the diagnosis was not verified. A liver injury seems most likely but it is difficult to say whether there was a central or a subcapsular rupture. The attacks of pain may have been due to increasing collection of blood under the capsule. The simultaneous tenderness in the liver region supports this explanation. On the other hand, the marked anemia indicates a larger loss of blood than could well be occasioned by a moderate hematoma in the liver. The repeated attacks of violent pain of short duration may well have been caused by blood clots in the biliary ducts.

In this case there is thus a possibility that there was a "hemobilia" with biliary colic caused by a subcapsular liver lesion. The probability seems somewhat less than in the two preceding cases.

DISCUSSION

Nine cases have been collected in which a trauma to the liver region has resulted in a hemorrhage into the biliary tract. A subcapsular lesion was proved by autopsy or operation in six of the cases (Cases 3 to 8). In the remaining three cases such a lesion seemed highly probable for the reasons mentioned. The presence of blood in the biliary tract was proved in three cases (Cases 1 to 3); it was highly probable in five (Cases 4 to 8) and at least possible in one (Case 9).

Considering that these nine cases have been taken from a collection of twenty cases and that blood in small quantities in the bile ducts is likely to be overlooked it seems justified to conclude that hemorrhage into the biliary tract or "hemobilia" is a frequent symptom in subcapsular liver lesions. (There have been cases described of central liver ruptures where there was no escape of bile, indicating that no bile radicals were injured [Robertson[27]]. One could not expect a hemobilia of importance in such a case.)

The course and the signs of hemobilia can be studied in the nine cases described.

In minor liver injuries, which although apparently not infrequent are seldom recognized because of their vague symptoms, a slight hemobilia could be expected to give an occult melena. In Case 1 where a hemobilia was verified, the test for occult blood in the stools was positive. It is recommended that this test be made in all cases where a liver injury is suspected, but where the symptoms are uncertain.

A more pronounced hemobilia causes hematemesis (Cases 3 and 6) or melena (Cases 2 to 6). A secondary anemia may result (Cases 1, 3, 5, and 9), sometimes severe (Cases 4 and 6).

It may be difficult to decide whether the hemorrhage originates in the digestive tract or in the liver (Case 6). The sudden increase in the venous pressure caused by the compression of the thorax which usually occurs in these cases may give rise to multiple small hemorrhages and to epistaxis (Cases 4 and 6). A protracted hemorrhage lasting for weeks or months is most likely to be due to hemobilia. The bile mixed with the blood delays clotting and the vessels in the liver parenchyma have little power of contraction.

If the blood clots in the biliary tract, new events occur.

The passage of the clots causes pain which has the character of biliary colic (Cases 1 to 4 and 7 to 9). The passage of a clot has been proved in a few cases where it was found in the vomit (Case 3) or in the stools (Case 2). When the clot has passed the attacks may stop definitely (Case 3), or until new clots are formed (Case 2). It seems that clots consisting of a mixture of blood and bile become rather tough in consistency (Cases 2 and 3).

When the clots do not pass but obstruct the ducts, jaundice naturally results as in Cases 2 and 7. It may subside when the clot passes.

I have not found any case where a permanent obstruction of the common duct was with certainty due to a coagulum. (Lincke[19] described a 6-year-old boy who was operated upon for a total obstruction and where there were signs of a central liver lesion. Although it is possible that the obstruction was caused by a coagulum, it seems equally possible that a constriction of the common duct was caused by a concomitant injury to the surrounding tissues.)

If the blood clots in the gall bladder it acts in the same way as a gallstone (Cases 1, 2, and 3), producing characteristic pain and tenderness. A distended gall bladder may be palpated (Cases 1 and 2). It is even probable that the clots will become impacted and cause a distention gangrene (Case 2).

As long as the blood flows freely from the rupture it is probable that no large cavity will be formed, but when the biliary ducts are closed off, fluid

collects and forms a cavity. This is clearly demonstrated in Cases 7 and 8 (probably also in Case 4). When the attacks of biliary colic subside the liver becomes enlarged and a continuous sensation of tenseness in the epigastrium results. Large cavities containing a mixture of bile and blood may be found upon operation or autopsy. In other cases a clot in a central duct may loosen and get pushed out with a large gush of blood (Cases 2, 3, and 4).

The symptoms of "hemobilia" have often been misinterpreted (Cases 1, 2, 4, 7, and 8). When this symptom is understood and the signs of it are looked for, a clearer conception and a more certain diagnosis of many cases of subcapsular liver lesions will be obtained.

SUMMARY

1. Nine cases (one reported herein and eight collected from the literature) of subcapsular liver injuries presenting a certain or probable hemorrhage to the biliary tract have been studied. This symptom has been named "hemobilia."

2. Hemobilia may cause (a) hematemesis and melena, (b) biliary colic, (c) biliary obstruction or (d) gall bladder distention.

3. Hemobilia should be looked for in all cases of liver injuries with vague symptoms. It might be a frequent symptom of value in the diagnosis and understanding of these cases.

REFERENCES

1. Ady, C.: Die Subkutanen Leberverletzungen, Dissert. Greifswald, 1900.
2. Andersson, L.: Ueber zentrale Leberrupturen und ihre Komplikationen, vorzugsweise Abscesse, Beitr. z. klin. Chir. **135**: 696, 1926.
3. Bauer, H.: Die zentrale Leberruptur und ihre Folgen, Vrtljschr. f. gerichtl. Med. **56**: 33, 1918.
4. Brandberg, R.: Beitrag zur Klinik der traumatischen Leberverletzungen bei unverletzter Kapsel, Acta chir. Scandinav. **63**: 321, 1928.
5. Brandberg, R.: Subkutana traumatiska leverskador, Nord. med. tidskr. **4**: 712, 1932.
6. Castrén, P.: Ueber subkutane Leberrisse und das hepatorenale Syndrom, Acta. chir. Scandinav. (suppl. 105) **93**: 1, 1946.
7. Corriden, T. R.: Subcapsular Rupture of the Liver in a Child, SURGERY **8**: 446, 1940.
8. Edler, L.: Die traumatischen Verletzungen der parenchymatösen Unterleibsorgane, Arch. f. klin. Chir. **34**: 343, 1887.
9. Finsterer, H.: Zur Diagnose und Therapie der Leberverletzungen, Beitr. z. klin. Chir. **119**: 598, 1920.
10. Fraenkel, F.: Ueber die subkutane Leberruptur und deren Behandlung durch primäre Laparotomie, Beitr. z. klin. Chir. **30**: 418, 1901.
11. Hawthorne, H. R., Oaks, W. W., and Neese, P. H.: Liver Injuries With a Case Report of Repeated Hemorrhages Through the Biliary Ducts, SURGERY **9**: 358, 1941.
12. Hitzrot, J. M.: Subcutaneous Injuries of the Liver, Ann. Surg. **66**: 50, 1917.
13. Holm, O.: Zur Kenntnis der zentralen Leberruptur, Dissert. Berlin, 1914.
14. Hämäläinen, M.: Ueber der Entstehungsmechanismus der durch stumpfe Gewalt verursachten sog. subkutanen Rupturen der parenchymatösen Organe des Unterleibes, Acta Soc. med. fenn; p. 6, 1925.
15. Klob: Cited by Bauer.[3]
16. Krogius, A.: Untersuchungen ueber den Mechanismus der traumatischen Organrupturen, Acta chir. Scandinav. **52**: 299, 1919.
17. Lecerf: Observation du kyste traumatique du fois, Union médicale, p. 94, 1881.
18. Lewerentz: Ueber die subkutane Rupture der Gallenwegen, Arch. f. klin. Chir. **71**: 111, 1903.
19. Lincke, Ad.: Ein weiterer Beitrag zur operativen Behandlung einer Gallengangszerreissung, Dissert. Leipzig, 1908.
20. Markwaldt: Ausgeheilte traumatische Ruptur der Leber, München. med. Wchnschr. p. 32, 1909.
21. Merkel: Zentrale Leberzertrümmerung, Ztschr. f. Med.-Beamte p. 112, 1913.
22. Norgore, M.: Traumatic Rupture of the Gall Bladder, Ann. Surg. **123**: 127, 1946.

23. Owen: Case of Lacerated Liver, London Med. Gazette, p. 1048, 1848.
24. Petersson, C.: Cited by Andersson.[2]
25. Rathcke: Subkutane Leberruptur, Berl. klin. Wchnschr. **35**: 718, 1898.
26. Robertson, D. E., and Graham, R. R.: Rupture of the Liver Without Tear of the Capsule, Ann. Surg. **98**: 899, 1933.
27. Robertson, D. E.: Rupture of the Liver Without Tear of the Capsule, Ann. Surg. **106**: 467, 1937.
28. Rudberg, H.: Traumatic Rupture of the Bile Ducts, Upsala läkaref. förh. **27**: 223, 1922.
29. Schweninger: Ueber Leberrisse, Deutsche med. Ztschr. **11**: 122, 1882.
30. Siegel, E.: Ein Fall von traumatischer Gangrän der Gallenblase, München. med. Wchnschr. **56**: 341, 1909.
31. Thöle, F.: Verletzungen der Leber und der Gallenwege, Stuttgart, 1912 (Neue Deutsch. Chir. IV), Ferdinand Enke.
32. Vance, B. M.: Subcutaneous Injuries of Abdominal Viscera, Arch. Surg. **16**: 631, 1928.
33. Wilms: Zur Behandlung der Leberrupturen, Deutsche med. Wchnschr. **27**: 564, 593, 1901.
34. Wright, L. T., Prigot, A., and Hill, Jr., L. M.: Traumatic Rupture of the Liver Without Penetrating Wounds, Arch. Surg. **54**: 613, 1947.
35. Wulsten, J.: Zur Klinik und Pathologie der zentralen Leberruptur, Beitr. z. Klin. Chir. **153**: 424, 1931.

In Memoriam

ALBERT O. SINGLETON

1882-1947

ALBERT O. SINGLETON, professor of surgery at the University of Texas School of Medicine, died at his home in Galveston on June 12, 1947, of coronary artery disease. He was widely known as an outstanding surgeon and medical educator and was, in addition, greatly beloved by many friends both within and outside the profession.

He belonged to a small group of surgeons, now rapidly disappearing in an age of increasing specialization, who could perform almost any type of operation well. He was also recognized as a leader in the adoption of new surgical techniques and procedures. He was an early advocate of upper intestinal decompression as a routine postoperative measure, and he realized the importance of maintaining proper fluid and electrolytic balance in his patients at a time when administration of parenteral fluids was considered a radical procedure. He was the first man in the state of Texas to perform a total gastrectomy, a pneumonectomy, and closure of a tracheo-esophageal fistula. Because of his vast amount of experience in many fields of surgery, he could write and talk authoritatively on a wide variety of subjects. His best known papers dealt with the problem of wound disruption, the use of anatomic incisions, cancer surgery of the large bowel, diseases of the lymphatics, splenectomy, and the newer aspects of thoracic surgery. He continually stressed the importance of fundamental anatomy, physiology, and pathology in the treatment of the patient, and felt that all progress in surgery must rest upon advances in these basic sciences. In addition to his medical writing, he was particularly interested in the history of medicine in Texas, and chose as his presidential address for the Southern Surgical Association in 1939, an account of "The Surgeon in the Romantic Story of Texas.

As a clinical teacher of surgery in the wards and as an operating room demonstrator, Dr. Singleton was at his best. He was a master technician, bold and decisive as an operator, but ever cautious in his handling of the tissues. His remarks were punctuated by wit and emphasized by brevity.

Dr. Singleton received his surgical training under Dr. James E. Thompson, having been granted his medical degree from the Medical Branch of The University of Texas in 1910. He was associated with the institution for thirty years, and was appointed professor of surgery and chief surgeon of the John Seally Hospital upon Dr. Thompson's death in 1927. He worked constantly for the betterment of the hospital and medical school and was instrumental in bringing to fulfillment a program of expansion of the physical plant as well as setting up the first postgraduate program in Texas for specialty training. Under his leadership, the departments of Orthopedics, Genitourinary Surgery, Thoracic Surgery, and Plastic and Maxillo-facial Surgery were set up and provisions were made for animal research. Because of his untiring efforts, the Medical School was able also to establish, a number of years ago, an Anesthesia Department of the first class.

A member of the Founder's Group of the American Board of Surgery, Dr. Singleton served on the Board of Governors of the American College of Surgeons from 1937 to 1940. He was also vice-president of the latter organization in 1939-1940, and had been president of the Southern Surgical Association, president of the Texas Surgical Society, and vice-president of the American Surgical Association. He was also a member of the editorial staff of SURGERY. He belonged, in addition, to the American Association of Thoracic Surgery, the International Surgical Association, the American Association for the Surgery of Trauma, the American Cancer Society, Kappa Sigma, Phi Alpha Sigma, and Alpha Omega Alpha. He was an active participant in organizational meetings, enjoying keenly the stimulation of association with surgical colleagues and contributing greatly himself to scientific discussion of surgical problems.

Albert O. Singleton

Dr. Singleton was genuinely devoted to his family and home. He is survived by his wife, the former Miss Will Dean Bivens, and by two sons, Dr. Albert O. Singleton, Jr., and Dr. Edward B. Singleton.

Dr. Singleton stood always for the highest personal and professional ideals. His name must be added to the list of illustrious surgeons in the Romantic Story of Texas. —*T. G. Blocker, Jr.*

Book Reviews

Aseptic Treatment of Wounds. Carl Walter, M.D. New York, 1948. The Macmillan Co.

This work will appeal to surgeons and nurses concerned with this important problem. The book represents a complete study of every phase of the subject. Most modern surgeons and nurses in charge of operating theaters have received their training from those who preceded them. The technical preparation of materials for use in the operating rooms and the principles of asepsis have been handed down from generation to generation without questioning the validity of the procedures. The surgeons and nurses at the beginning of the century were more intimately concerned with methods because they were the practical testers of the laboratory theories. They scrutinized the techniques with care and with understanding of the underlying purpose of each step. As tested techniques developed they were accepted or discarded. By the time of World War I the majority of these surgical preparations and procedures had been standardized for general use with only minor variants in certain clinics.

Walter's book traces the historical development of the aseptic principle. The step-by-step progression from the first recognition of the infectious nature of sepsis to the complete triumph of steam sterilization is expounded with accuracy and complete documentation. Facsimile title pages of the important first discoveries lend interest to the manuscript.

The clinical destruction of bacteria is carefully considered. The estimation of the value of given chemicals against the various types of microorganisms is presented with the proper measures necessary to really define their worth. The common antiseptic chemicals such as alcohols, chlorinated compounds, iodine, formaldehyde, the mercurials, the phenols, and the quaternary ammonium compounds are all compared as to their value against bacteria in varied situations. The chemical disinfection of instruments is treated from a practical every-day standpoint. Technical details to avoid contamination of sterilized instruments are well illustrated. This makes the book an ideal reference book for training younger members of the medical and nursing professions. The care necessary to maintain the cutting edges of instruments is well considered. Sterilization of utensils, ampules, rubber goods, instruments with optical lenses, plastics, brushes, suture materials, etc., is made clear, and possible mistakes in their handling pointed out.

The use of physical agents to destroy bacteria is reviewed. The effects of light, pressure, radiation, dry and moist heat are given consideration. Sanitization by boiling water is rated as important. The construction of sterilizers so that there is proper venting with mechanisms to prevent backflow contamination is shown by numerous drawings. No step is too unimportant to safeguard the sterility of the prepared materials.

Sterilization by steam has many pitfalls but these are unmasked. The types of steam sterilizers are compared. Their advantages and disadvantages are set forth. Mistakes in using superheated steam are pointed out. The control of steam sterilization and methods for testing are carefully tabulated.

Sterilization of dressings and dry goods is illustrated by packaging for a laparotomy. The complete picture is presented from the preparation of the wrapper, the assembling of supplies, the wrapping and tying of the kit, even to the type of knots—amply illustrated step by step. The steps in folding laparotomy sheets, gowns, the making of sponges, pads, packs, etc., are beautifully shown. No operating room or nursing school should be without this book because of the detailed information it provides.

The care of instruments, their sterilization, the care of hollow needles and glass syringes, dry and wet techniques for rubber gloves, and every phase of preparation of materials for aseptic surgery is explained clearly so that nothing is left to chance.

Complete details of every conceivable type of operative procedure are given from the scrubbing of the team, the preparations of the nurses' tables, the disposal of the instruments, the donning of the gowns and gloves, the disinfection of the operative field, the draping of the area, the positioning of the patient, and the actual operating room technique in the

aseptic handling of material even to the placing of the sutures. These maneuvers are given line drawing treatment omitting no detail which may help to clarify. Measures to diminish the air-borne contaminants are discussed under such headings as masking, aerosols, and ultraviolet light installations.

The last chapters of the book are concerned with the decontamination and resterilization of instruments and goods after septic cases. Measures to determine that contamination will not be spread are again well shown by illustrations. The preparation of parenteral fluids so that these are convenient and easy to use has long been one of Walter's pet projects. No director of a central preparation room or Red Cross blood procurement center can afford to pass up the wealth of information given in these chapters on solutions and blood and plasma facilities. The control measures necessary to prevent the spread of communicable disease from one part of the hospital to another are also well covered. The final chapter has to do with the proper maintenance of sterilizing equipment. It is replete with many useful suggestions gained by intimate firsthand observations under actual running conditions.

Books Received

The receipt of books is acknowledged in this section and this treatment must be regarded as sufficient acknowledgment of the courtesy of the senders. Selections will be made for more extensive review dictated by the interests of our readers and as space permits.

OSTEOTOMY OF THE LONG BONES. By Henry Milch, M. D., Consulting Orthopedist, Maimonides Hospital. Cloth. Price $6.75. Ed. 1. Pp. 320, with 269 illustrations. Springfield, Ill., 1947, Charles C Thomas, Publisher.

A SHORT HANDBOOK OF PRACTICAL ANAESTHETICS. By Höel Parry-Price, Surgeon Commander, U. D., R. N. U. R. Cloth. Price $3. Ed. 1. Pp. 120, with 50 illustrations. Bristol, 1946, John Wright & Sons, Ltd.

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